

CIP/RDT&E Issue



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June 1972

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The issuance of this publication approved in accordance with NAVEXOS P-35.

NAVMED P-5088



from the Chief

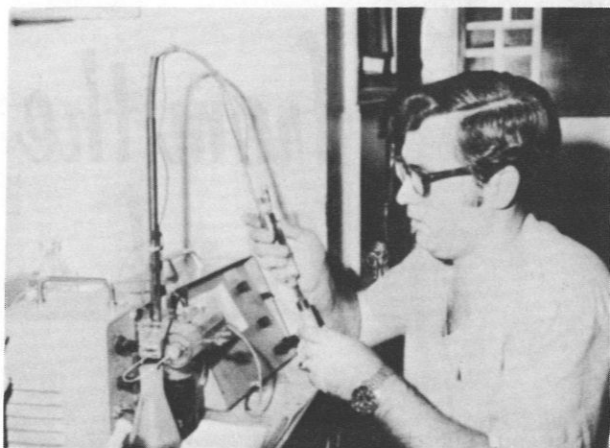
This issue of U.S. NAVY MEDICINE inaugurates the annual publication of a joint review of the Clinical Investigation Program (CIP) and the Research, Development, Testing and Evaluation (RDT&E) program.

A study of this review gives some indication of the broad spectrum of professional interests being pursued at our medical activities, whether patient-oriented, military mission-oriented, or both, for future application of acquired skills and knowledge is often multi-dimensional.

For some time RDT&E has made useful, sometimes unique, contributions to science. I consider the CIP a great step forward in the support of our training efforts and most important in the delivery of the highest quality of medical and dental care. Additional benefits in professional satisfaction, recruitment and retention of Navy physicians and dentists are anticipated.

All members of the Navy Medical Department are urged to take an active interest and participate in our research-investigational programs. As a vital link to modern medicine and improved patient care, such endeavors will not pass unrewarded.

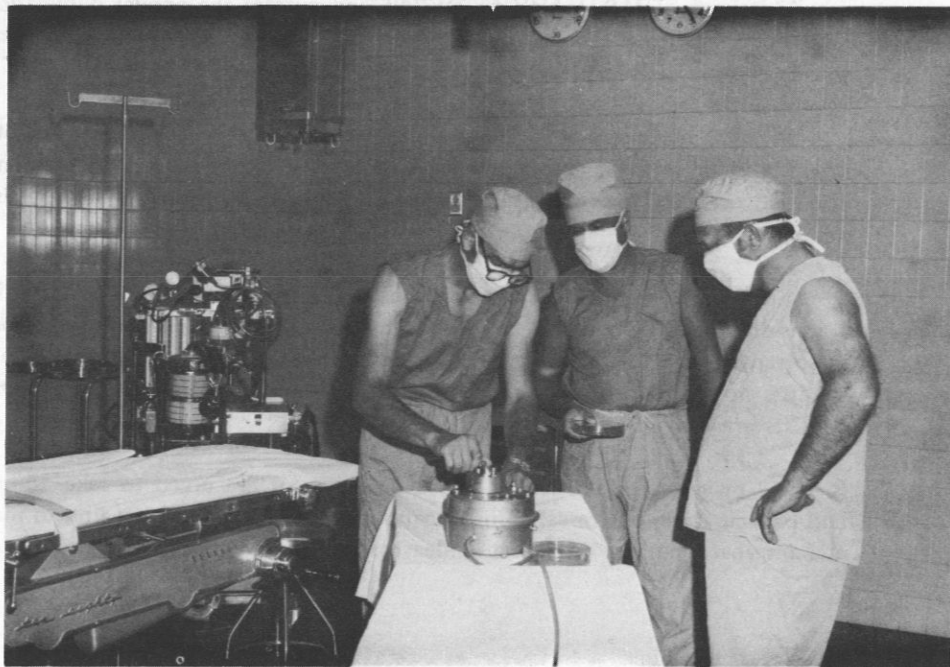




HM1 Rickey D. Kirby, Senior Instructor of Cardiopulmonary School, Naval Hospital Corps School, San Diego, Calif., demonstrates a blood-gas analyzer for cardiopulmonary students. HM1 Kirby was elected as one of the two California delegates to the National Society of Cardiopulmonary Technologists, Inc. He is also serving a three-year term as vice-president of the San Diego Chapter of Cardiopulmonary Technologists. (Courtesy of HMCM J.D. Johnson, USN, Nav Hosp Corps School, San Diego, Calif.)



During one of the daily MEDCAPS established by the CAP, a Navy corpsman is pictured treating burns on a small boy in the village of Quang Xuyen in 1970.



HMC G.W. Hatcher, PMT Course Instructor, (left) is shown instructing LCDR G. Taylor, MSC, USNR-R, 12th N.D. (center), and HM1 A. Crawshaw, USNR, 9th N.D. (right) in techniques for air sampling in an operating room. Ten Naval Reserve Medical Dept. personnel were charter members of the first two-week Training Course on Control of Infections in Hospitals conducted at Nav Hosp Oakland, Calif., 1-14 Aug 1971. The course was designed to acquaint participants with the magnitude and complexity of problems in hospital-associated infections, and covered recommended standards/procedures for surveillance, prevention and control of infections. (Courtesy of CDR N.C. La Chapelle, MSC, USN, Chief, Preventive Medicine Service, Nav Hosp Oakland, Calif.)

NAVY HOSPITAL CORPS

June 17, 1898-1972

The occasion of the 74th Anniversary of the Navy Hospital Corps is an excellent time to look to the future of the Corps, where it is headed, and what we must do to continue the traditions and excellence of the past 74 years.

As we move towards a zero draft goal, it is incumbent on all of us, particularly our senior Hospital Corpsmen, to motivate, train and counsel for retention the very best of our young Hospital Corpsmen. We must exert every effort to make these young men and women aware that, as important members of the Navy Health Care Team, they can enjoy a professionally rewarding career.

On this 74th birthday of the Corps the opportunities available to each of you surpass those of any previous time. To help you advance in your chosen profession we are turning increasingly towards the accreditation of our training programs by civilian teaching institutions. The paramedical specialties long available to members of the Corps have become increasingly important to the practice of medicine in our civilian medical and dental communities. The part-time outservice training programs leading to degree certification have been vastly expanded to enable our young men and women, both Hospital Corpsmen and Dental Technicians, to keep educationally abreast of their civilian contemporaries.

My birthday message to each of you is that we care about you and your future. I know each succeeding year will find the Hospital Corps efficiently carrying out its mission and, as in the past, ever respected by those it serves so very well. Happy Birthday!



G. M. DAVIS
Vice Admiral, MC, USN
Surgeon General

From the Assistant Chief For Research and Military Medical Specialties



RADM Ralph E. Faucett, MC, USN

The research division of the Bureau of Medicine and Surgery welcomes this opportunity to present the abstracts of studies performed at naval hospitals throughout the United States.

Until quite recently, all research conducted in the hospitals was under the sponsorship of RDT&E funds. With the inception of the Clinical Investigation Program, the focus has changed. Now the vitality of hospital "research" depends primarily on the Clinical Investigation Program. RDT&E interest centers on specific efforts to answer militarily relevant problems and to provide support to the research laboratories. The joint funding by these programs should foretell a new era of increased productivity in naval hospitals.

From the Director, CICC*

RADM George H. Reifenstein, MC, USNR



This is the first publication of abstracts of studies conducted under provisions of the (CIP) Clinical Investigation Program (BUMEDINST 6000.4).¹ It represents "a small step forward for man but a giant step" for the Navy Medical Department.

On 17 Jul 1971 a call for study proposals to be submitted by 1 Sept 1971, was issued. The BUMED CICC carefully reviewed priorities set by Clinical Investigation Review Centers (CIRCs) for 189 proposals; it approved 125, and in Oct 1971 it authorized allocation of nearly all of the \$400,000 O&MN (Operations and Maintenance, Navy) funds and an additional \$117,000 of OPN (Other Procurement, Navy) funds. These CIP abstracts represent the first progress reports submitted annually on 1 Feb to CICC. Since these CIP studies have only recently been initiated, less emphasis can be placed on results observed now, but considerable importance can be attached to the fact that this annual publication of abstracts has begun.

This abstract compendium demonstrates the value of clinical investigation to the Navy by: relating investigation to training and patient care, aiding investigators in exchange of information, and achieving added professional status for the Navy Medical Department. Like blood flow, pulse pressure and tissue nourishment, the ultimate benefits cannot accrue at headquarters but will be realized at peripheral points — the participating clinical investigators in hospitals where patients receive improved care.

Investigators were asked to indicate the subsection in which abstracts should properly be classified. Some of these were changed at CICC to reflect content rather than originating department. Obviously, cross classification was not feasible; instead, an alphabetical index of investigators is provided for cross reference on page 61.

Abstracts of approved RDT&E on-going Work Units which are conducted at our CONUS hospitals are included in this review and are to be distinguished from CIP studies. Although RDT&E (Work Units) and CIP studies complement each other, it was felt that identification of these studies by CIP and RDT&E designations should be made to emphasize that the funding, relevancy criteria, and submission procedures differ. Accordingly, a CICC number appears following CIP abstracts and RDT&E abstracts are indicated by their Project numbers (M-----).

RDT&E Work Units are funded from research funds appropriation, while CIP studies are authorized out of O&MN and OPN dollars. CIP submission requirements are contained within BUMEDINST 6000.4 series; RDT&E submission provisions are listed in BUMEDINST 3900.3 series.

Twenty-six subspecialties have been identified for the classification of CIP/RDT&E abstracts. A page index of these categories is provided on page 6.

Comments will be welcomed by the Editor of U.S. NAVY MEDICINE and the Director, CICC. The BUMED CICC now is permanently located in Tower 18, NNMC, Bethesda, Md., 20014. Telephone: (301) 295-0584 and -0585; Autovon 295-0584 and -0585.

*CICC — Clinical Investigation Control Center

1. See U.S. NAVY MEDICINE, 58:44-45, Aug 1971.

CIP and RDT&E

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ANESTHESIOLOGY

THE EFFECT OF GENERAL ANESTHESIA ON THE OXYGEN CAPACITY OF BLOOD. M.S. Jakubowski; M.W. Wofford; L.T. York and C.R. Valeri. Naval Hospital, Boston.

The effect of general anesthetic agents on the oxygen carrying capacity of the red blood cell is being studied. Measurements include P_{50} determination by two independent methods and red cell 2,3-diphosphoglycerate (2,3-DPG) measurement. Red cell metabolism and 2,3-DPG production is stimulated with a solution of pyruvate, inosine and glucose. Preliminary data shows that halothane may have an effect on 2,3-DPG metabolism with questionable direct effect on P_{50} . CICC 2-02-109

EFFECT OF OSMOTIC DIURESIS ON DURATION OF NEUROMUSCULAR BLOCKADE INDUCED BY NON-DEPOLARIZING MUSCLE RELAXANTS. C.H. Lockhart and W.M. McDermott. Naval Hospital, Portsmouth, Va.

Osmotic diuresis is sometimes necessary during

anesthesia involving the use of the non-depolarizing muscle relaxants curare and gallamine.

As the excretion of these drugs is predominantly by renal mechanisms, it is postulated that this diuresis might significantly shorten their duration of action.

Currently, under barbiturate anesthesia and controlled ventilation, curare or gallamine is being administered to cats, and the magnitude and duration of paralysis is being measured. At a later date, the procedure will be repeated on the same animal adding mannitol to the regimen.

CICC 2-08-502

DETERMINATION OF SENSITIVITY TO SKELETAL MUSCLE RELAXANT IN NERVE INJURIES. R.E. Tobey. Naval Hospital, Bethesda.

Hyperkalemia following succinylcholine administration in patients with neural injury has been demonstrated in this study. The potential complication is cardiac arrest and death, especially in patients with a central nervous system lesion. Non-depolarizing muscle relaxants (d-tubocurarine and gallamine) were shown not to produce hyperkalemia in these patients.

M4305.05-3037AGG2

EFFECT OF ANESTHETIC AGENTS ON PLATELET AGGREGATION. **M.W. Wofford; M.S. Jakubowski; L.T. York and C.R. Valeri.** Naval Hospital, Boston.

This study was undertaken to determine the effects of anesthetic agents on platelet aggregation. Fresh whole blood is equilibrated with various concentrations of halothane, and 5% carbon dioxide in compressed air at 37°C. Aggregation of platelets in platelet-rich plasma was studied using standard methods. Preliminary data indicates that halothane, *in vitro*, inhibits platelet aggregation.

CICC 2-02-115

CARDIOVASCULAR DISEASE

EVALUATION OF THE EFFECTS OF ACUTE INFARCTECTOMY ON POST-INFARCT ARRHYTHMIAS. **B.L. Aaron and W. Hix.** Naval Hospital, Portsmouth, Va.

The effect of excision of acutely infarcted areas of myocardium upon control or relief of intractable arrhythmias is to be evaluated.

An experimental dog model will be used with documentation of the extent of infarction, type and responsiveness of arrhythmias to standard treatment followed by infarctectomy for intractable arrhythmias. Pertinent parameters are the further course of the arrhythmia(s) and survival from the acute infarction.

The project is not yet underway pending arrival of the necessary equipment.

CICC 2-08-511

EFFECT OF ANESTHETIC AGENTS ON ATRIO-VENTRICULAR CONDUCTION IN THE INTACT DOG HEART. **J.L. Atlee, III; C.A. Bush and R.E. Tobey.** Naval Hospital, Bethesda.

Halothane has been shown, in studies employing His's bundle electrograms, to depress A-V conduction in dogs. The effects of other anesthetic agents on A-V conduction, as measured by His's bundle electrograms, are also being studied. Different agents may vary in their effects on A-V conduction.

An agent such as halothane should be used with caution in conditions where impaired conduction exists or may be implicated as a cause of arrhythmias.

CICC 2-06-321

ALTERATIONS IN THE RENAL CLEARANCE OF DIGOXIN AS MODIFIED BY VOLUME LOADING, ALKALINIZATION, AND DIURETICS AND MEASURED BY A RADIOIMMUNOASSAY TECHNIQUE.

D.D. Brown and J. Dormois. Naval Hospital, Pensacola.

Renal excretion of digoxin is a major determinant of the plasma levels of digoxin. Previous experimental data suggests that digoxin is handled by glomerular filtration plus a component of tubular reabsorption, and that digoxin clearance bears a relatively linear correlation with creatinine clearance.

This investigation, using hospitalized patients and a radioimmunoassay technique for measuring plasma and urinary digoxin concentrations, will attempt to delineate the changes in the ratio of digoxin clearance to creatinine clearance produced by "volume" loading with mannitol, alkalization with sodium bicarbonate, and/or diuresis with furosemide.

CICC 2-8-525

SAPHENOUS VEIN GRAFTING IN CORONARY REVASCULARIZATION. **T.L. Folkerth; R.G. Fosburg and J.W. Hammon, Jr.** Naval Hospital, San Diego.

In clinical situations where autologous saphenous veins are not available for coronary artery bypass procedures, preserved allograft veins might serve as acceptable functional substitutes.

Twenty-one dogs have undergone ascending aorta to left anterior descending coronary artery bypass grafting under cardiopulmonary bypass. Autogenous veins were employed in seven, while 14 received allograft jugular veins, ten of which were processed in Hank's solution and four of which were freeze-dried and irradiated. Twelve of 21 surviving animals, who lived from two days to 2½ months, were subjected to postoperative coronary arteriography; occlusion of the vein-coronary artery anastomosis in all animals was demonstrated. The study suggests that graft occlusion is related to disparity in size of the recipient vessel and the graft.

CICC 2-16-402

EFFECTS OF OSCILLATION OF PERIPHERAL BLOOD FLOW IN POSTOPERATIVE PATIENTS.

L.C. Getzen. Naval Hospital, San Diego.

Over 750 postoperative patients were treated with oscillating motion. These patients were either obese, chronically debilitated or had undergone a peripheral vascular surgical procedure. There were no pulmonary vascular thromboembolic complications. By contrast, postoperative thromboembolic complications occurred

in 10% of the patients who underwent similar surgical procedures at this hospital.

The investigator has observed a conservation of the peripheral muscle mass, increased peripheral oxygenation without increasing the respiratory tidal volume and an earlier discharge date in patients who were oscillated postoperatively.

MR041.20.01-0253AGX

THE POST-EXERCISE ISCHEMIC S-T SEGMENT — A TREADMILL STUDY. P. Goldfinger; S.C. Smith, Jr. and C.W. Shaeffer. Naval Hospital, Portsmouth, Va.

The purpose of this study is to define the characteristics of the post-exercise ischemic S-T segment as seen in patients with coronary heart disease subjected to treadmill stress testing. Results will be compared with those obtained by atrial pacing in the same patients.

This study has not yet begun pending arrival of equipment.

CICC 2-08-506

A PROSPECTIVE ANALYSIS OF THE VALUE OF AN INTERMEDIATE CORONARY CARE UNIT (ICCU) IN THE MANAGEMENT OF PATIENTS WITH ACUTE MYOCARDIAL INFARCTION. P. Goldfinger; S.C. Smith, Jr. and C.W. Shaeffer. Naval Hospital, Portsmouth, Va.

The purpose of this study is to determine the usefulness of an intermediate coronary care unit. A special facility adjacent to the coronary care unit will be utilized to follow patients with acute transmural myocardial infarction. Telemetry monitoring will be used, and coronary care unit personnel will manage the patients.

The study is in progress, and no conclusions are presently available.

CICC 2-08-513

THE EFFECTS OF PLURONIC F-68 ON CARDIOVASCULAR MECHANICS, REGIONAL BLOOD FLOW AND SMALL VESSEL PATENCY. F.L. Grover; J.R. Warden; D.G. Amundsen; B.F. Gibbs and R.G. Fosburg. Naval Hospital, San Diego.

Arterial injuries and hemorrhagic shock are frequently encountered in the care of combat and civilian casualties. Pluronic F-68, a nonionic, nontoxic surface active agent, has been shown to decrease blood viscosity and platelet adhesiveness and to increase microcirculation in hemorrhagic shock. The purpose of this investigation is to determine therefore, if the

administration of Pluronic F-68 will: increase the patency rate following small arterial surgery; increase blood flow to various organ systems in shock states; increase cardiac output in shock states; alter pulmonary artery and systemic pressure and resistance in shock.

Three groups of dogs (six each) will undergo femoral endarterectomy, one group being infused with saline intra- and postoperatively for 24 hours, another with low molecular weight dextran and the third with Pluronic F-68. Femoral arteries will be examined for patency and degree of thrombus formation at the end of 24 hours.

Two groups of dogs (nine each) will be bled to a mean arterial blood pressure of 50 mm Hg, with monitoring of cardiac output, pulmonary artery pressure and resistance, and blood flow through the carotid artery, thoracic and abdominal aorta, and renal arteries, before and after the intravenous injections of Pluronic F-68 in group I and saline in group II.

MR041.20.01-0376A2CE

ANGIOGRAPHIC ANALYSIS OF LEFT VENTRICULAR MECHANICS IN YOUNG PATIENTS WITH ATYPICAL CHEST PAIN AND ISCHEMIC HEART DISEASE. A.D. Hagan and J.R. Morgan. Naval Hospital, San Diego.

A better system of classifying young persons with suspected ischemic heart disease is urgently needed. It is important to understand the complex and detailed aspects of ventricular function to form the basis for this classification. The result of such accurate classification could result in the saving of substantial amounts of Government monies required for the direct care of such persons, disability remuneration and the necessity of obtaining suitable replacements for those disabled.

Young patients being evaluated for suspected ischemic heart disease by the cardiology service at this hospital will be subjected to a thorough analysis of ventricular function by such methods as cardiac catheterization and angiography, as well as standard clinical and laboratory parameters for evaluation of such pathology. Abnormalities of left ventricular mechanics will be carefully studied in those subjects with normal coronary arteriograms in an effort to identify the most significant parameters for the recognition of impaired left ventricular function.

There is no report of progress as this program is new.

MR041.20.01-0379A2GJ

PHYSIOLOGY AND TREATMENT OF SHOCK FOLLOWING BATTLE TRAUMA. C.M. Herman. Naval Medical Research Institute, Bethesda.

Defective O₂ transport to and utilization by tissues is a common feature of shock following trauma. Using baboons as experimental animal models, the mechanisms by which tissue hypoxia brings about adaptive changes in delivery of O₂ to the tissues by the red blood cell will be explored. An increase in RBC O₂ delivery (P₅₀ of the oxyhemoglobin-dissociation curve) after acute blood loss and during other tissue hypoxic states has been shown to be associated with an increase in levels of creatine, 2,3-DPG, and other phosphate metabolites in the red cell.

In another approach to the basic mechanisms involved in the cellular damage occurring in shock, the means by which gram-negative endotoxin suppresses the cardiovascular system are under investigation. A rat ventricular myocardium model is used to assess the effect of endotoxin on contractility of the heart. It has been found that endotoxin has no depressing effect on the ability of this preparation to respond to electric stimulation without the additional presence of factors present in fresh serum.

One current theory of shock holds that endotoxin enters the circulation because of the development of splanchnic ischemia, and this endotoxemia then becomes the cause of irreversible cardiovascular depression. A new Limulus lysate bioassay technique has been applied to studies of hemorrhagic shock in baboons; resulting data indicate that splanchnic ischemia and resultant endotoxemia are not features of hemorrhagic shock in the subhuman primate and are most likely peculiar to canine shock models.

MR041.20.01-0287A2GE

SYSTEMS' RESPONSE TO POST-TRAUMATIC HEMORRHAGIC AND SEPTIC SHOCK. C.M. Herman. Naval Medical Research Institute, Bethesda.

Pulmonary failure continues to be a major cause of death following initial successful resuscitation from combat trauma. The etiology of this problem remains unknown, but a number of possibilities have been considered. It has been proposed that particulate material, which forms in bank blood during storage, is filtered out by the lung during transfusion and causes pulmonary complications. A series of baboons have been transfused with 21-day-old ACD bank blood, in a volume equal to three times the shed blood volume after two hours of hemorrhagic shock. Measurements of pulmonary artery pressure, pulmonary vascular resistance, cardiac output, and pulmonary gas exchange

have shown no effect of these massive transfusions on pulmonary function. The lungs are nearly free of any particulate matter or vascular blockage at autopsy. On the basis of these experiments, blood transfusion does not appear to cause pulmonary damage following hemorrhagic shock.

Other experiments, to determine the effect of different aspects of the management of shock and trauma, have been completed. Pulmonary failure has not been produced by resuscitation from hemorrhagic shock employing either saline plus red cells, 5% albumin plus red cells, or whole blood alone. Acute gram-negative sepsis, created by intravenous infusion of live *E. coli* organisms, has not been associated with any predictable signs of pulmonary damage. Various models for peritonitis and pelvic abscess have not been uniformly effective in producing a type of pulmonary failure suitable for study. The type of anesthesia and state of sedation control the interpretation of animal experiments.

M4305.05-3007BGGO

RESPIRATORY AND MICROCIRCULATORY DEFECTS OF TRAUMA. L.D. Homer; C.M. Herman and R. Tobey. Naval Medical Research Institute, Bethesda.

Acutely ill patients suffering from the consequences of severe injury, blood loss and infection, frequently present precariously marginal cardiovascular and pulmonary function. Physicians managing such patients can be assisted by detailed information concerning sudden changes in the patient's state.

The system to be developed will use an on-line computer for physiological monitoring and evaluation. It will be aimed towards a non-invasive technique, avoiding the necessity for indwelling catheters. Mathematical models of respiration will be used to compute cardiac output and V/Q imbalance of the lung from acquired data on the flow and composition of expired gases. The possible value of this approach in patient monitoring will be assessed through animal experiments. Concurrent measurements of cardiac output, pulmonary shunting, capillary filtration, capillary red cell velocity, and acid-base balance can be obtained in animal subjects by more direct methods which are less suitable for use in patients.

MR12.524.016-0001AG2E

DETECTION OF OCCULT VENOUS THROMBOSIS BY AN IMPEDANCE METER AND 125 FIBRINOGEN. W.C. Johnson; H.W. Fegley and R.L. Mullin. Naval Hospital, Boston.

The incidence of pulmonary emboli in the postoperative patient may be as high as 15% in certain "high risk" groups. Often these emboli come from extremities that do not present clinical evidence of venous thrombosis. The incidence of occult venous thrombosis in the postoperative patient is not known.

Two techniques have recently been developed that may serve to detect venous thrombosis; these are the Impedance Phlebograph and 125 labeled fibrinogen. This investigation will evaluate each of these techniques for reliability and will determine the risk for occult venous thrombosis in postoperative patients.

To date several patients have been studied by the impedance phlebograph, and the apparatus functions satisfactorily. The small number of patients treated so far precludes any valid statistical analysis of the data. CICC 2-02-101

PREVENTION OF POSTOPERATIVE VENOUS THROMBOSIS BY ASPIRIN, DEXTRAN, COUMADIN AND INTERMITTENT COMPRESSION UNIT. W.C. Johnson; H.W. Fegley and R.L. Mullin. Naval Hospital, Boston.

Pulmonary embolism is a significant postoperative complication and is probably the leading cause of death in the postoperative period for patients who do not have extensive myocardial disease. In certain "high risk" groups, the incidence of pulmonary emboli may be 15% and that of venous thrombosis, 30%.

This investigation will study the effect of various therapeutic modalities on the incidence of venous thrombosis and pulmonary emboli. "High risk" elective surgical patients will be randomized into five therapy groups: (1) aspirin treated, (2) dextran treated, (3) Coumadin treated, (4) intermittent extremity compression and (5) control. Previous studies dealing with the reduction of venous thrombosis have usually been based on a clinical diagnosis that is unreliable in about 30% of the cases and does not take into account occult venous disease. This limitation is eliminated in the present study by the use of a new noninvasive diagnostic technique of impedance phlebography. The investigation has just been initiated.

CICC 2-02-102

ARTERIALIZATION OF THE VENOUS SYSTEM. W.C. Johnson. Naval Hospital, Boston.

The ability to reverse the arterial and venous flow to an organ or limb has never been fully evaluated. Root has reported success in arterialization of the popliteal venous system in dogs. Benefits of such a reversal of flow would be realized in severely ischemic limbs or possibly in mesenteric insufficiency.

The investigator plans to study several different models of reversal, i.e. reversal of the isolated perfused canine kidney with subsequent reimplantation of the kidney, and similar maneuvers with a segment of small intestine. Other models that may warrant study will also be investigated.

CICC 2-02-104

TREATMENT OF ACUTE AND CHRONIC EDEMA SECONDARY TO LYMPHATIC OR VENOUS INSUFFICIENCY. W.C. Johnson; H.W. Fegley and R.L. Mullin. Naval Hospital, Boston.

Periodically patients are seen who are severely disabled by a large edematous extremity. The etiology of the edema may vary: venous, lymphatic, idiopathic, or a combination of these. The classical mode of therapy consisting of bed rest, elevation and diuretics requires long hospitalization, and, early recurrence is frequent.

A therapeutic unit for the exclusive treatment of edematous extremities has been established. Patients will be treated by a Jobst intermittent compression machine. Following reduction in the edema, a Jobst elastic support will be worn to maintain the reduction in edema. Several patients have been evaluated to date. CICC 2-02-106

PATHOGENESIS OF ENDOTOXIN SHOCK IN MILITARY MEDICINE (FELINE). J.L. Kitzmiller. Naval Hospital, San Diego.

The project evaluates the role of intravascular coagulation and complement activation as pathogenetic mechanisms in a feline endotoxin shock model. Cats were defibrinogenated with Arvin fractionated from Malayan pit viper venom and were then given a standard dose of *E. coli* endotoxin. Hemodynamic and metabolic responses of normal and defibrinogenated cats were similar — hypotension and acidosis. All cats died. The experiments did not support the concept of an essential role for fibrin formation in mediating endotoxin shock.

Cobra venom factor was used to reduce the complement titer of cats to zero and these animals were then given endotoxin. Pretreated and normal cats

responded with leukopenia, thrombocytopenia, hypotension, acidosis and death. We conclude that this model fails to support the hypothesis that the injurious effects of endotoxin are due to complement activation. MR041.20.01-0351A2HX

PATHOGENESIS OF ENDOTOXIN SHOCK IN MILITARY MEDICINE (PRIMATE). J.L. Kitzmiller. Naval Hospital, San Diego.

This current project extends the feline endotoxin shock studies to baboons. The role of fibrin formation in the pathogenesis of primate sepsis is being explored by prior removal of all fibrinogen with Arvin.

Baboons will be decompartmentalized with cobra venom factor prior to infusion of living *E. coli* microorganisms. The mechanism of possible beneficial effects of corticosteroid administration will be evaluated by monitoring any changes such treatment may produce in the hemodynamic, hematologic and metabolic responses to endotoxin in baboons. Emphasis is placed on changes in plasma levels of lysosomal enzymes in endotoxin shock in treated and normal animals.

M4305.05-3066AGG2

EFFECTIVENESS OF BETA BLOCKADE IN IMPROVING EXERCISE TOLERANCE IN CORONARY DISEASE. R. Landesman and G.S. Francis. Naval Hospital, Great Lakes.

The plan is to study patients with known coronary artery disease employing treadmill submaximal exercise testing before, and after, six weeks of therapy with blocking doses of propranolol.

CICC 2-13-019

LONGITUDINAL STUDY OF CORONARY ARTERY DISEASE AND MYOCARDIAL REVASCULARIZATION SURGERY. D.A. Lee. Naval Hospital, Bethesda.

Although myocardial revascularization surgery is applicable for the alleviation of severe angina pectoris, this form of treatment has not been proved to prolong life or reduce the incidence of myocardial infarction. The purpose of this study is to provide sound bases for selecting patients for operative treatment of coronary artery disease.

Long-term clinical follow-up will be obtained in several hundred patients with angiographically-defined coronary lesions. An attempt will be made to correlate natural history with angiographic disease patterns and with various clinical parameters. Long-term

results of saphenous vein bypass surgery will also be obtained.

At the present time 100 patients have entered the study, 40 of whom have had surgery. Less than one year follow-up is currently available in the majority of patients and the acquired data do not yet allow any conclusion relative to long-term efficacy of saphenous bypass surgery or to methods for selecting patients for this form of therapy.

CICC 2-06-315

MYOCARDIAL REVASCULARIZATION FOR ISCHEMIC HEART DISEASE. J.J. McHale, Jr.; B.M. Shepard and M. Mills. Naval Hospital, Bethesda.

We will determine if the poor prognosis associated with coronary artery occlusive disease can be reversed by myocardial revascularization. Morbidity, mortality and long-term survival following an acute myocardial infarction and/or the onset of angina pectoris have been well documented and accurately presented in the literature. Many in the military have symptomatic coronary artery occlusive disease. The economic gain in preventing death and disability in active duty personnel and restoring these men to duty is obvious.

An operation utilizing various combinations of saphenous vein bypass grafts, from the aorta to the coronary arteries, is being performed on selected patients.

To 1/6/72 we have performed 43 revascularization procedures. There have been two operative deaths (within one month of operation), accounting for a mortality rate of 4.6%, with no operative deaths in the past 12 months. There has been one late death. Sixteen of the 42 patients (38%) have been active duty personnel and eleven of these patients have been returned to duty. The clinical result in 35 of 42 patients is excellent thus far (i.e. full activity without symptoms). We are convinced that myocardial revascularization is a significant step forward in the treatment of coronary artery disease.

CICC 2-06-316

EVALUATION OF TISSUE PRESERVATION TECHNIQUES RELATED TO AORTIC HOMOGRAFT VALVES. J.J. Oury; J.W. Hammon, Jr., and M.J. O'Sullivan, Jr. Naval Hospital, San Diego.

The objective is to determine the ideal method of preservation for aortic allograft valves in the treatment of military patients. Canine aortic valves will be evaluated, after being mounted on a metal-teflon support ring and preserved by tissue culture media, as products

of controlled freezing with cryo-protective agents. The experimental model will include transplantation into a suitable canine recipient of the opposite sex. At specific intervals animals will be killed and valves evaluated by immunofluorescent and cytotoxic antibody assay, plus conventional histopathologic and tissue culture techniques.

A series of twelve animals have had mitral valve replacements with viable aortic allografts and are currently being evaluated by the aforementioned techniques.

M4305.05-3074AGJ2

CORRELATION OF EXERCISE TESTING AND CORONARY ANGIOGRAPHY. H.J. Palay and R. Landesman. Naval Hospital, Great Lakes.

Submaximal exercise tolerance testing will be done on each patient undergoing coronary arteriography (if it is deemed clinically appropriate) using the bicycle ergometer. The anatomic abnormalities will be correlated with the ECG changes. The predictive value of submaximal exercise tolerance testing will be assessed. CICC 2-13-002

CORRELATION OF LEFT VENTRICULAR HEMODYNAMICS AND EXTENT OF CORONARY DISEASE. H.J. Palay and R. Landesman. Naval Hospital, Great Lakes.

In an effort to demonstrate the effect of the extent of coronary artery disease on ventricular function, each patient undergoing coronary arteriography will undergo studies of rest and exercise hemodynamics. The project will begin when investment equipment has been installed.

CICC 2-13-003

BEDSIDE STUDY OF CVP AND WEDGE PRESSURE IN ACUTE MYOCARDIAL INFARCTION. H.J. Palay and G.S. Francis. Naval Hospital, Great Lakes.

The frequent disparity between left and right heart filling pressures in myocardial infarctions is being studied using the Swan-Ganz catheter. Insufficient patients have been studied to reach a conclusion.

CICC 2-13-011

ASSESSMENT OF LEFT VENTRICULAR FUNCTION IN MYOCARDIAL INFARCTION USING NON-INVASIVE TECHNIQUES. H.J. Palay and G.S.

Francis. Naval Hospital, Great Lakes.

Patients admitted to the Coronary Care Unit with myocardial infarction will be evaluated serially with recording of left ventricular ejection time, pre-ejection period, isovolumic contraction time and indicator dilution cardiac output. The study will begin when phonocardiographic equipment has been updated.

MR041.20.01.0369A2GJ

MOVEMENT OF INTRAVENTRICULAR SEPTUM IN TAMPONADE. H.J. Palay. Naval Hospital, Great Lakes.

The plan is to study with ultrasound the movement of the intraventricular septum in patients with tamponade, in an effort to delineate the mechanism of the paradoxical pulse. Studies have been insufficient for analysis to date.

MR041.20.01.0370A2GJ

EVALUATION OF THE CARDIORESPIRATORY EFFECTS OF PERHEXILINE IN PATIENTS WITH ANGINA PECTORIS. C.J. Pepine and L. Wiener. Naval Hospital, Philadelphia.

The hemodynamic and myocardial metabolic effects of a new non-nitrate, non B-blocker anti-anginal agent, perhexiline, were studied in eleven angina pectoris (AP) patients with angiographically proven coronary heart disease. Left ventricular (LV) responses to exercise and atrial pacing, with and without perhexiline, included measurements of LV filling pressure, stroke work index (SWI), heart rate (HR) and systemic pressure (SPm). Perhexiline did not alter resting HR ($76.4 \pm 3.3 \rightarrow 74.5 \pm 3.0$ b/min.), mean \pm SEM (standard error of the mean), or SPm ($100.9 \pm 3.9 \rightarrow 103.2 \pm 3.3$ mmHg), while SWI increased ($51.7 \pm 2.8 \rightarrow 65.6 \pm 7.6$ Gm-m/b/m²) and LV filling pressure decreased ($15.8 \pm 3.0 \rightarrow 10.0 \pm 3.1$ mmHg). During exercise at identical work loads SWI increased similarly ($85.5 \pm 14.6 \rightarrow 86.5 \pm 12$) but at lower LV filling pressure ($34.0 \pm 3.9 \rightarrow 15.0 \pm 3.3$) $p < .01$ and HR ($119 \pm 7.7 \rightarrow 106 \pm 5.2$) $p < .05$, without changing SPm ($125 \pm 10 \rightarrow 126 \pm 4$) while AP was either not evoked or delayed. With controlled atrial tachycardia perhexiline enhanced myocardial lactate extraction ($-4.5 \rightarrow 9.0\%$) $p < .05$, while oxygen extraction was unchanged ($62.7 \pm 3.0 \rightarrow 67 \pm 2.7\%$) at similar HR ($126.5 \pm 5.3 \rightarrow 127.1 \pm 4.1$) and SPm ($109.6 \pm 5.9 \rightarrow 106 \pm 3.6$).

These data suggest that perhexiline reduces myocardial ischemia and ischemia-related LV dysfunction (\downarrow SWI/LV filling pressure). This study further indicates that perhexiline appears to offer the beneficial effects of both nitroglycerin (\downarrow LV filling pressure) and propranolol (\downarrow HR) without their undesirable actions (nitroglycerin \uparrow HR and propranolol \downarrow SWI/LV filling pressure).

CICC 2-05-602

PATHOGENESIS OF CARDIOVASCULAR DISEASE IN PATIENTS WITH DIABETES MELLITUS. C.J.

Pepine and C.R. Bemiller. Naval Hospital, Philadelphia.

Diabetes mellitus is commonly associated with severe premature symptoms of atherosclerosis. The presence of diabetes and its relation to clinical, hemodynamic, coronary arteriographic, and metabolic features will be explored in patients undergoing diagnostic cardiac catheterization studies. In addition, a continuing perspective, long-term, follow-up study is anticipated. This investigation has not been in progress long enough to present data or warrant conclusions at this time.

CICC 2-05-607

TREATMENT OF ANGINA PECTORIS WITH CARDIOSELECTIVE BETA-ADRENERGIC BLOCKADE.

C.J. Pepine and L. Wiener. Naval Hospital, Philadelphia.

The success of propranolol (P) in treating angina pectoris (AP) has led to the development of beta-adrenergic blocking agents with a more favorable ratio of beta receptor blocking action to intrinsic myocardial depression. Comparison of the effects of these agents on left ventricular (LV) function may clarify the basis for P's anti-anginal action. LV end-diastolic pressure (EDP), dp/dt, stroke work index (SWI), and heart rate (HR) were measured at rest and during exercise with and without AY 21011 (10 mg), KO 1313 (10 mg), KO 1366 (2.5 mg) or P (10 mg) intravenously in 46 patients with angiographically proven coronary heart disease.

Significantly depressed LV function (\downarrow SWI/LVEDP) during exercise was not observed with AY 21011 (SWI/EDP -4.8% from control), KO 1313 (+5.9%), and KO 1366 (+2.2%), whereas P markedly depressed SWI/EDP -32% ($p < .01$). Exercise LV dp/dt declined with AY 21011 (-12.2%), KO 1313 (-19%) and KO 1366 (-18%); this related to significant ($p < .05$) reduction of exercise HR (AY 21011 -11%, KO 1313 -10.8% and KO 1366 -15.6%). P's depression of LV dp/dt (-31%) could not be attributed solely to its modest

attenuation (-7.3%) of exercise HR. AY 21011 reduced the intensity or delayed the onset of AP in six of 12 patients, KO 1313 in three of 12, KO 1366 in one of 6, but P was effective in 14 of 16 patients.

Intrinsic myocardial depression induced by P appears to be a major factor associated with its anti-AP properties. Depressed LV function may account for P's more favorable anti-anginal effect when compared to more potent beta blockers.

CICC 2-05-612

MANAGEMENT OF INTRACTABLE ANGINA PECTORIS (AP). C.J. Pepine and C.R. Bemiller.

Naval Hospital, Philadelphia.

Recent enthusiasm generated by early success of aortocoronary bypass surgery for AP emphasizes the need for objective evaluation of the course of patients treated with medical therapy alone. Accordingly, clinical, hemodynamic and coronary arteriographic studies were obtained in 81 male patients (mean age 46.2 years) with refractory, incapacitating AP. All were treated with conventional measures in addition to propranolol. After 34.8 months, 7.5% had died. Of the survivors: five sustained myocardial infarctions, AP increased in six and was unchanged in three; improvement occurred in 62 (76.5%).

After 24.6 months ten patients were restudied. Comparison of left ventricular (LV) function under identical conditions showed no significant differences; (original study \rightarrow restudy): heart rate 123.2 \rightarrow 120.8; LV end-diastolic pressure 28.8 \rightarrow 24.9; stroke work index 110 \rightarrow 106; LV dp/dt 2680 \rightarrow 2400. Coronary cine angiographic abnormalities progressed in four of ten patients. In these patients advancing disease correlated with myocardial infarction or increased AP during the inter-study interval. In the remaining patients unchanged LV function and coronary angiography were associated with symptomatic improvement.

These observations indicate that propranolol may enhance survival in symptomatically improved patients unrelated to objective angiographic or hemodynamic improvement. Since the majority of patients with refractory AP can be benefited by propranolol, justification for surgical revascularization in this group is open to question.

MR041.20.01-0016A2GX

THE EFFECTS OF THE ATRIAL PUMP ON VENTRICULAR FUNCTION. C.J. Pepine; C.R. Bemiller and S.J. Schang. Naval Hospital, Philadelphia.

The effect of atrial systole on myocardial function and metabolism was evaluated in 13 patients with atrial fibrillation undergoing cardiac catheterization studies before and after reversion to sinus rhythm. Left ventricular (LV), end-diastolic pressure (EDP), LV systolic pressure (LVSP), LV dp/dt, and heart rate were measured. Simultaneous coronary sinus-arterial blood samples were analyzed for lactate and oxygen extractions. Atrial pacing was used postconversion to match the preconversion heart rate.

Postreversion LV function (LV stroke work index/LVEDP) increased, but the changes were not significant. Myocardial lactate extraction per unit oxygen extraction decreased at similar tension time index. It would seem that atrial systole improves hemodynamic function with deterioration of metabolic function. These results are very preliminary and preclude any valid conclusion at this time.

MR041.20.01-0060A2GX

EVALUATION OF "FALSE MASTER'S TEST". C.J. Pepine and C.R. Bemiller. Naval Hospital, Philadelphia.

Typical angina (A) may be present without significant coronary artery obstruction with typical ischemic ECG changes. Thirty-one patients (mean ages 43.7 years) with A, myocardial abnormalities, and normal coronary arteriograms have been followed. Nine cases had typical, 22 atypical A. Ten had abnormal serum lipids (Type IV in six, Type II in four); abnormal GTT was noted in seven. An atrial sound in six and minimal cardiomegaly in three patients were noted. Nineteen had resting ECG abnormalities: 15 nonspecific S-T segment changes, two left bundle branch block, two left axis deviation. Rest to exercise hemodynamics revealed increased left ventricular (LV) end-diastolic pressure in 21 patients (mean $11.2 \pm 2.6 \rightarrow 26.1 \pm 6.1$ mmHg) ($p < .05$) while stroke work index increased (+12%). LV contractility assessed by LV dp/dt (mean $1340 \pm 210 \rightarrow 2710 \pm 700$ mmHg/sec.) and LV angiography were normal. LV ischemia was detected by abnormal lactate extraction with atrial pacing (in 12), or > 1 mm S-T segment depression during exercise (in 15 patients).

After a mean follow-up of 3.8 years, 26 patients managed with propranolol noted marked improvement of A syndrome. No changes in hemodynamics or anatomy were noted in five restudied patients. Autopsy on one patient who died suddenly revealed normal coronary arteries and myocardium. Complications

of ischemia, i.e. progression of symptoms, infarction, and heart failure were absent in the remaining patients. The fate of patients with A and normal coronaries, with LV abnormalities (ECG, metabolic, or hemodynamic), appears favorable. Their A, usually atypical and frequently incapacitating, responds to propranolol. Long-term preliminary observations suggest a nonprogressive disorder.

MR041.20.01-0132A2GX

RESPIRATORY MECHANICS IN ANGINA PECTORIS (AP). C.J. Pepine and L. Wiener. Naval Hospital, Philadelphia.

Since left ventricular (LV) dysfunction during myocardial ischemia incident with AP is well-documented, secondary alterations in lung mechanics could relate to these symptoms. To evaluate the possibility of a pulmonary mechanical basis for part of the syndrome of AP, we examined airway resistance (R_{aw}), lung volume (TGV), and lung compliance (C_L) during AP.

AP patients (24) with coronary heart disease but without bronchopulmonary disease or congestive heart failure were studied. LV hemodynamic and ECG responses were recorded prior to, during, and after relief of pacing-induced AP. C_L and body plethysmographic measurements of R_{aw} and TGV were made under similar conditions. AP was associated with a sudden increase in LV end-diastolic pressure (EDP), mean +41%, $p < .01$, without change in end-diastolic volume (EDV). LV distensibility (EDV/EDP) decreased abruptly (-37%, $p < .01$), accompanied by reduction in airway conductance ($1/R_{aw}/TGV$) -40%, $p < .05$, while C_L declined (-27%, $p < .05$). When AP was relieved by cessation of pacing, these changes returned toward pre-angina levels. Likewise, if AP was relieved by nitroglycerin despite persistent atrial pacing, pulmonary mechanics returned to normal. Our data indicate that periods of myocardial ischemia induce LV dysfunction and produce an abrupt increase in LVEDP. The resulting increase in pulmonary capillary pressure and congestion effects lung mechanical alterations (R_{aw} , hyperinflation, and reduced C_L). The ensuing change in ventilatory effort may be interpreted as chest tightness, heaviness, or constriction.

MR041.20.01-0133A2GX

PREVENTIVE CONTROL OF HYPERLIPEMIA. C.J. Pepine and L. Wiener. Naval Hospital, Philadelphia.

Coronary heart disease (CHD) is frequently associated with hyperlipemia (H). It may be possible to attenuate this generally progressive disease by control

of serum lipids. D-thyroxine in combination with propranolol, which blocks the beta-adrenergic mediated hyperkinetic effects of thyroid hormone, was evaluated as a means of controlling H and possible progression of CHD.

Thirty patients with CHD and H were hospitalized for clinical evaluation including lipid profile, resting and exercise ECG, coronary arteriography, and left ventricular hemodynamic measurements. They were treated with increasing doses of D-thyroxine (mean dose 8 mgm/day) utilizing propranolol (mean dose 480 mgm/day) to control undesirable hyperkinetic effects. A detailed diary of the frequency and severity of their symptoms and lipid determinations were recorded at monthly intervals. Patients received complete annual reevaluations, and, where clinically indicated, objective hemodynamic and angiographic reassessment. Patients (5) who met the criteria as outlined but declined therapy, served as controls.

Results indicate that a significant decrease in serum cholesterol (31%) and triglycerides (20%) occurs, while signs of factitial hyperthyroidism are absent. Two patients have been restudied and reveal no evidence of progression of CHD.

MR041.20.01-0146A2GX

USE OF DIGITALIS AND PROPRANOLOL. C.J. Pepine and L. Wiener. Naval Hospital, Philadelphia.

Heart failure often limits the usefulness of beta-blocking agents especially in patients with arrhythmia or angina. Since digitalis inotropism is independent of adrenergic activity, the effect of incremental doses of acetylstrophanthidin (AS) alone, and after propranolol (P), was studied in 24 intact dogs. Left ventricular pressures, dp/dt, and aortic flow velocity (AVF) were recorded before and after AS 0.025 mg/kg, a digitalizing dose. P (0.5 mg/kg) was infused in 12 dogs following initial AS dose. Then, all dogs received additional AS (0.025 mg/kg) at 15-minute intervals. Heart rate was maintained (atrial pacing) at pre-AS rate and measurements were made until ventricular tachycardia (VT) supervened. The initial AS dose increased V max (dp/dt/K [P-LVEDP] extrapolated to 0) $1.91 \pm 0.18 \rightarrow 3.02 \pm .34$ ml/sec. and AVF $78 \pm 10 \rightarrow 102 \pm 16$ cc/sec. Subsequent AS increased V max (3.62 ± 138) until VT at $0.078 \pm .011$ mg/kg AS. P initially reduced V max ($3.98 \pm .42$) and AVF (110 ± 18), prior to VT. Accordingly, P delayed VT and permitted a larger cumulative AS dose (0.106 ± 0.18 mg/kg) $p < .05$.

These data indicate that P-induced myocardial depression is significantly ($p < .01$) reversed by the

independent positive inotropism of cumulative doses of AS as VT is suppressed. Consequently, in clinical conditions where beta-blockade is desirable, P may be used despite the presence of heart failure if additional glycoside is administered.

MR041.20.01-0188A2GX

ASYMPTOMATIC CORONARY ARTERY DISEASE (CAD) IN YOUNG MALES. C.J. Pepine and L. Wiener. Naval Hospital, Philadelphia.

The incidence of sudden death in latent coronary heart disease (CHD) is estimated at 65%. Identification of patients at risk is difficult since lipid profile and other screening techniques measure potential rather than actual CHD. Thus, a study was undertaken to characterize the coronary anatomy and electrocardiogram (ECG), hemodynamic, and myocardial metabolic responses of young asymptomatic "coronary-prone" patients. Twelve patients (mean age 38.8 years [9 Type II and 3 Type IV hyperlipoproteinemia]) were studied by standardized submaximal exercise ECGs, left ventricular (LV) catheterization, and coronary arteriography.

Hemodynamic measurements at rest, during atrial pacing and exercise, including stroke index, LV end-diastolic pressure (EDP), and LV dp/dt max were normal except for two patients (LVEDP 22 and 24 during exercise). Abnormal myocardial lactate metabolism detected in five patients corresponded with an abnormal exercise ECG in three. Exercise ECGs were normal in the remaining nine. Coronary arteriography demonstrated significant CAD ($> 50\%$ obstruction) in eight of 12 patients. No correlation is evident between the extent of CAD and hemodynamic or ECG abnormalities in these asymptomatic patients.

It is apparent that advanced CAD can exist in asymptomatic young males, and that ECG and hemodynamic stress tests are insensitive to these patients. While analysis of blood lipids may have epidemiologic and long-range predictive value, coronary arteriography is required to detect the presence of significant CAD among high-risk patients.

MR041.20.01-0363A2GJ

TREADMILL EXERCISE TEST PERFORMANCE IN A GROUP OF PATIENTS SIX MONTHS POST-MYOCARDIAL INFARCTION, CORRELATION WITH DIAGNOSTIC CORONARY ARTERIOGRAPHY. C.W. Shaeffer; S.C. Smith, Jr.; R.G. Daly and P. Goldfinger. Naval Hospital, Portsmouth, Va.

Treadmill exercise testing will be performed under controlled conditions on all patients with a previous diagnosis of acute myocardial infarction, returning for evaluation after a period of limited duty. The test results will be correlated with clinical findings. Coronary arteriography will be performed on a limited number of the patients who present positive and negative exercise responses. The roles of coronary collateral circulation and limited vessel involvement will be assessed in determining the test results.

CICC 2-08-505

A REVIEW OF CORONARY CARE UNIT EXPERIENCE AT A LARGE MILITARY TEACHING HOSPITAL, 1967-1971. C.W. Shaeffer; S.C. Smith, Jr. and P. Goldfinger. Naval Hospital, Portsmouth, Va.

Experience in a Coronary Care Unit at a 1500-bed military hospital will be reviewed. Analysis of acute myocardial infarction in a relatively young mean age population will be completed. Clinical characteristics of this somewhat atypical group will be compared with other CCU experience.

CICC 2-08-512

RADIOIMMUNOASSAY OF SERUM DIGOXIN (DIG). J. Sode; F.M. Walsh; A.G. Levy and W.V.R. Vieweg. Naval Hospital, Bethesda.

The utility of DIG assays in clinical work is under study in several laboratories. We have measured DIG by radioimmunoassay using commercial reagents in serum, urine and saliva. At recommended incubation times of 30 min. equilibrium was reproducible, although slightly higher values resulted with longer incubations.

In evaluating DIG levels in clinical samples, we observed a wide scatter among patients on comparable oral glycoside doses and found levels greater than 3 ng/ml in three nontoxic patients. It subsequently became apparent that many of these samples were drawn by our house staff within the first few hours after administration of DIG.

Others have stressed the importance of sample timing and have published serum concentration curves after oral DIG in normal subjects. We measured serum DIG serially in six patients on maintenance therapy.

Expressed as % of baseline, mean DIG levels $\frac{1}{2}$, 1, $1\frac{1}{2}$, 2, 4, 6 and 8 hours after the daily oral dose were 167, 185, 228, 256, 172, 145 and 134% respectively. These levels declined with the accepted half-time for DIG (34 hr.) between 6 and 24 hr. after the dose. Urinary DIG/mg creatinine rose after the dose, indicating an increase in the DIG filtration load.

The data emphasize that when serum DIG levels are used as an index of digitalization, blood samples should be obtained just prior to the daily dose and in no instance sooner than six hours following ingestion of the drug.

CICC 2-06-313

DERMATOLOGY

CHARACTERIZATION OF THE INVERTED FOLLICULAR KERATOSIS. B.L. Johnson; J.F. Russo and W.A. Schrader. Naval Hospital, Philadelphia.

The purpose of this study is to define the inverted follicular keratosis on a histologic and histochemical basis and to place this keratosis in the proper classification with other keratotic lesions and cutaneous neoplasms.

Keratotic lesions from the surgical pathology rounds have been reviewed; to date 30 inverted follicular keratoses have been collected. Comparative light microscopy and histochemical studies of this group and other cutaneous tumors possessing similar features, in order to permit more accurate differentiation, are in progress. Statistical data as to age, sex predilection, predominant site of occurrence, clinical presentation, and duration are also being compiled.

MR041.20.01-0347A2GX

FALSE POSITIVE VDRL IN MILITARY RECRUITS. W.A. Schueller. Naval Hospital, San Diego.

Numerous papers have been published concerning transient biological false positive Venereal Disease Research Laboratories (VDRL) tests secondary to immunizations and vaccinations. Most deal with smallpox vaccination, but some relate to other types of immunizations.

This study will determine the incidence of false positive VDRL reactions in military recruits undergoing the current battery of routine immunizations and prophylactic medications.

Recruits at the Marine Corps Recruit Depot at San Diego will be utilized. VDRL tests will be drawn at

specified intervals throughout their routine training and the resulting data will be statistically analyzed.
CICC 2-16-404

ENDOCRINOLOGY — METABOLISM

SERUM CORTISOL AFTER ABRUPT CESSATION OF SHORT-TERM HIGH-DOSE STEROID THERAPY.
S.M. Fidler; R. Hines; E. Perlin; R.B. Moquin and J. Sode. Naval Hospital, Bethesda.

MOPP (Mustargen, Oncovin, procarbazine & prednisone) is a popular chemotherapeutic combination for patients with advanced Hodgkin's Disease. In these immunosuppressed patients even transient impairment of the hypothalamic-pituitary-adrenocortical axis would constitute an increased risk. Therefore we evaluated the rapidity with which serum cortisol levels returned to normal after abrupt withdrawal of MOPP.

Six patients who received 70-100 mg/day of prednisone for 14 days were studied. Prior to MOPP, mean serum cortisol for the group was 17.8 mcg% in A.M. and 5.7 mcg% in P.M. During MOPP, cortisol suppressed to less than 4 mcg% in all patients. After abrupt cessation of MOPP, mean serum cortisols for four of the six patients were 2.6, 6.0, and 18.1 mcg% respectively on day 1, 2 and 3 after steroid withdrawal. The fifth patient reached pre-treatment levels on day 2. The sixth patient developed a febrile illness on day 2 and responded to this stress with serum cortisol levels of 23.0 mcg% in A.M. and 25.9 mcg% in P.M. Thus resumption of spontaneous ACTH secretion was evident by the third day after the withdrawal of MOPP in all six patients. No symptoms of adrenocortical insufficiency were noted during the two days after withdrawal when serum cortisol levels were low.

It appears that suppression of serum cortisol after short-term high-dose steroid treatment lasts approximately two days and is well tolerated clinically. However it would seem reasonable to postpone elective stressful procedures until at least the third day after withdrawal.

CICC 2-06-304

ALDACTONE IN PRIMARY ALDOSTERONISM.
S.M. Fidler and J. Sode. Naval Hospital, Bethesda.

In primary aldosteronism the antihypertensive response to Aldactone has been invoked as a diagnostic test as well as a predictive index for surgical correction of hypertension. We recently studied a 26-year-old

male with aldosteronoma who was given a 10-week preoperative course of 400 mg/day of Aldactone. During this period his blood pressure (BP) fell from 190/120 to 118/84, and his serum potassium (K) rose from 2.9 to 4.7 mEq/L. It was noted, however, that at the end of this period he had developed an 8-lb. weight loss, a rise in blood urea nitrogen (BUN) from 12 to 29 mg/100 ml and a plasma volume deficit of 1000 ml as measured by radioiodinated serum albumin (RISA). Plasma renin activity (PRA) measured by rat bioassay and expressed as angiotensin II had risen from an initially suppressed level of 73 ng/100 ml (erect and on low Na intake) to 1000 ng/100 ml. Following volume repletion BUN decreased to 8 mg/100 ml and BP remained normal. Surgery was uneventful. PRA determined 1 and 3 weeks postoperatively was 236 and 291 ng/100 ml, respectively. Postoperative hyperkalemia was not observed.

These observations suggest that in patients with aldosteronoma preoperative treatment with Aldactone may hasten recovery of the suppressed renin-angiotensin-aldosterone axis, and thereby lessen the danger of postoperative hyporeninemia with hyperkalemia. Such treatment, however, may induce significant volume depletion in some patients. When the BP response to Aldactone is used as a predictive index for surgical correction of hypertension due to aldosteronoma, one must therefore ascertain that this fall in BP is not simply a manifestation of drug-induced hypovolemia.

CICC 2-06-322

DECREASED CALCIUM ABSORPTION (CaAb) ON CHOLESTYRAMINE THERAPY. **S.M. Fidler; W.M. Beckner; R.B. Johnson and J. Sode.** Naval Hospital, Bethesda.

Published reports on the effect of cholestyramine on CaAb are few and controversial. In the rat, no effect on CaAb was found despite the induction of steatorrhea and malabsorption of tritium-labeled Vitamin D. In contrast, Briscoe and Ragan (Amer. J. Clin. Nutr. 13:277, 1963) reported increased CaAb in three patients receiving 16 g/day of cholestyramine.

We have studied a 51-year-old male with idiopathic hypercalciuria and recurrent Ca-oxalate stones, who was receiving intermittent cholestyramine therapy (10-20 g/day) for severe pruritus complicating chronic active hepatitis. This therapy did not induce steatorrhea.

CaAb was determined from the ratio of oral/I.V. fractional ⁴⁷Ca retention measured by whole body counter. Ionized Ca was determined by Orion

electrode. Studies were done on a 0.4 g/day Ca diet and normal activity. Results while off and on cholestyramine therapy were as follows:

	OFF	ON
Total serum Ca (mg%)	9.3	9.3
Ionized serum Ca (mM/L)	1.1	1.05
Serum Phosphorus (mg%)	3.6	4.0
Urinary Ca (mg/24 hr.)	370	250
Calcium absorption (%)	85	67

The data show that cholestyramine therapy in conventional therapeutic doses may alter Ca absorption in man in the absence of steatorrhea.

CICC 2-06-325

TRANSVENTRICULAR HYPOPHYSECTOMY. C.B. Early and J. Sode. Naval Hospital, Bethesda.

A method of pituitary ablation, significantly more simple than any other presently available, is being developed. A Seldinger wire is passed through a small twist drill opening in the frontal skull, and guided under fluoroscopic control into the cerebral lateral ventricle, thence through the foramen of Monro, the third ventricle, down into the infundibular recess and pituitary stalk, into the hypophysis of a monkey. The wire is electrically insulated, except for its tip embedded in the hypophysis. Radiofrequency electrical current is then passed through the wire to effect pituitary ablation.

The efficacy of the ablation procedure is evaluated by assessing the degree to which pituitary function is eradicated, as determined by endocrine analyses.

CICC 2-06-333

SPECIFIC METABOLIC EFFECTS OF VARIOUS TYPES OF INJURY TO THE LIVER. D.E. Hutchison.

Naval Hospital, Oakland.

Liver recovery after trauma may be judged by its ability to accomplish certain anabolic functions, e.g., gluconeogenesis (formation of glucose from lactate). Following a control lactate tolerance test (LTT), 2 mEq/Kg, liver blood supply was interrupted and the organ thoroughly flushed (750 ml) with saline (4°C) for 15 minutes. A second LTT was performed with simultaneous blood samples drawn from the portal and hepatic veins for assay of glucose, lactate and pyruvate. Liver biopsy samples for glycogen determination were obtained also at the beginning and end of each test period.

Preliminary findings indicate that severe hyperglycemia and lactic acidosis follow liver ischemia. In an

attempt to lessen this complication, fasted dogs (to eliminate glycogenolysis and enhance gluconeogenesis) will be studied, and the liver perfusate will be buffered and oxygenated.

MR041.20.01-038A2GH

GROWTH HORMONE RESPONSE TO EXERCISE AS A TEST OF PITUITARY FUNCTION IN CHILDREN. B.S. Keenan; L.B. Kilmer and J. Sode. Naval Hospital, Bethesda.

Since human growth hormone (HGH) is available for treatment of some deficient patients, it is clinically important to recognize HGH deficiency in children of short stature. Definitive diagnosis of HGH deficiency requires at least two tests of HGH secretion, usually an insulin tolerance test and an arginine tolerance test. In children, these tests usually require hospitalization and involve some risk.

Strenuous exercise has been shown to be a potent stimulus to HGH secretion. We therefore evaluated the HGH response to a standardized exercise protocol in 25 healthy children of short stature who were not HGH deficient. Mean \pm SE (standard error) HGH values for the group were: resting 5.7 ± 1.0 ng/ml; 20 min. after exercise 11.8 ± 1.5 ng/ml; and 40 minutes after exercise 10.5 ± 1.7 ng/ml. The mean maximal values for the test, 13.7 ± 1.7 ng/ml, compared favorably with other provocative tests of HGH secretion. Of the 25 children tested, 24 (96%) had HGH values of 6 ng/ml or greater, and 21 (84%) had values of 7 ng/ml or greater.

It is suggested that this exercise test is a reliable and near maximal stimulus to HGH secretion. It has the following clinical advantages: it can be done on only three blood samples, in the outpatient clinic, and without the administration of any drug.

CICC 2-06-324

CONTROL OF SECRETION OF PARATHYROID HORMONE IN NORMAL ADULTS. R.E. Reitz.

Naval Hospital, Oakland.

The development of a sensitive radioimmunoassay for human parathyroid hormone (HPTH) and the use of a human hormone standard has enabled us to define the normal concentrations of HPTH in peripheral blood.

Mean HPTH at 0800 in 59 normal adult subjects was 292 ± 124 pg/ml standard deviation (SD). (Range: 125 to 670 pg/ml). HPTH concentrations in six subjects on a 200 mg calcium, 650 mg phosphorus diet at 0200, 0800 and 1600 hours were 350 ± 178 ,

339 \pm 107 and 398 \pm 168 pg/ml (mean \pm SD). EDTA (ethylenediamine tetraacetic acid) -induced hypocalcemia caused a mean 264% increase in HPTH (301 to 891 pg/ml) with a range of 73% to 740%. Calcium infusion resulted in a mean decrease of 41% (333 to 150 pg/ml). There was a linear inverse correlation between serum calcium and HPTH concentration ($y = 3341.7 - 302.6 x$), with a correlation coefficient of -0.71 . HPTH concentrations in 14 patients with primary hyperparathyroidism were significantly elevated compared to normal (mean 2936 \pm 3862 pg/ml vs. 292 \pm 124 pg/ml).

Conclusions: (1) Normal circulating concentrations of HPTH have been defined. (2) No diurnal variation in HPTH was observed. (3) HPTH concentration is inverse to serum calcium concentration. (4) There was definite separation between HPTH concentration in normals vs. hyperparathyroid subjects.
MR005.20.01-0341A2HX

ROLE OF PARATHYROID HORMONE IN THE HYPERCALCEMIA OF THYROTOXICOSIS. R.E. Reitz and C. Bochra. Naval Hospital, Oakland.

Human parathyroid hormone (HPTH) was measured by radioimmunoassay in four patients with thyrotoxicosis and hypercalcemia. Diagnosis of hyperthyroidism was established by elevated protein bound iodine (PBI), Thyroxine (T4) by column, and radioactive iodine uptake. Mild hypercalcemia (10.9 \pm 0.26 mgm%, mean \pm SD) (standard deviation) was noted in all four patients on a normal calcium (Ca) diet, and was slightly lower (10.4 \pm 0.45 mgm%) on a 200 mgm Ca diet. Mean HPTH levels at 8 a.m. and 4 p.m. (0.29 \pm 0.10 ng/ml and 0.35 \pm 0.08 ng/ml respectively) in hyperthyroid subjects were decreased slightly compared to normal subjects (0.40 \pm 0.19 ng/ml, and 0.53 \pm 0.16 ng/ml). Assessment of HPTH response was carried out with Ca infusion (10 mgm/Kg/3 hours) and EDTA (ethylenediamine tetraacetic acid) infusion (40 mgm/Kg/1 hour). Ca infusion in hyperthyroid subjects resulted in a 57% decrease in HPTH, compared to 56% decrease in normal subjects. EDTA-induced hypocalcemia resulted in a significant increase in HPTH secretion in all hyperthyroid patients (147 \pm 98%), which was similar to normal subjects (287 \pm 211%).

Conclusions: (1) Mean HPTH levels at 8 a.m. and 4 p.m. in hyperthyroid patients with hypercalcemia were decreased compared to normals, suggesting HPTH suppression by hypercalcemia. (2) Acute alterations in HPTH secretion in hyperthyroid and normal subjects produced by Ca and EDTA infusion were similar. (3) HPTH secretion does not appear to be a major

factor in the hypercalcemia associated with hyperthyroidism.
MR005.20.01-0341A2HX

ROLE OF FREE FATTY ACIDS IN GROWTH HORMONE REGULATION DURING FASTING. R.E. Reitz; R.L. Weinstein; H.V. Werner and P. Cianci. Naval Hospital, Oakland.

The effect of nicotinic acid (NA) administration (100 mg IV q 15 min) on mean plasma levels of free fatty acids (FFA), growth hormone (GH), cortisol (F) and glucose was determined before and after a 72-hour fast in five healthy adult males. NA administration in the fed state further decreased normal levels of FFA (.41 \rightarrow .21 mEq/L), while levels of GH (2.0 \rightarrow 1.7 ng/ml), F (15.1 \rightarrow 12.0 μ g%) and glucose (87.6 \rightarrow 90.0 mg%) showed no significant change. In the fasted state, NA suppression of elevated levels of FFA (1.46 \rightarrow .67 mEq/L) into the normal range (.4 \rightarrow .8 mEq/L) was accompanied by marked elevations of GH (3.0 \rightarrow 27.6 ng/ml), while levels of glucose (66 \rightarrow 68 mg%) showed no significant change, and plasma F (15.1 \rightarrow 9.8 μ g%) did not rise. To elucidate this observed rise in GH, metabolic clearance rate (MCR) of GH (mean \pm SD) was determined in three fasted healthy adult males before (132 \pm 7.5 L/24 hr) and after (138 \pm 7.9 L/24 hr) NA suppression of FFA.

Conclusions: (1) NA suppression of normal FFA levels during the fed state resulted in no rise in plasma levels of GH. (2) NA suppression of elevated FFA levels during fasting promoted a marked rise in plasma GH levels. (3) The rise in GH is explained neither by hypoglycemia nor a nonspecific stress response since plasma glucose remained unchanged and F levels showed no rise during NA administration. (4) Enhanced pituitary secretion of GH accounts for elevated plasma levels since no decrease in MCR occurred during NA administration. These elevations indicate a possible feedback role of FFA in the regulation of GH in fasting man.

MR005.20.01-03002HX

THIAZIDE DIURETICS IN THE DIAGNOSIS OF HYPERPARATHYROIDISM. J.J. Sabol; J. Sode and J.J. Canary. Naval Hospital, Bethesda and Georgetown University School of Medicine.

The use of thiazide diuretics in the diagnosis of hyperparathyroidism was evaluated by studying the calcemic effects of these drugs in a group of patients with intermittently or minimally-elevated serum

calcium levels. During thiazide administration elevations of serum calcium into the clearly abnormal range were observed in ten of the twelve patients in the study group. Following removal of the parathyroid adenomas the hypercalcemic response to thiazides was lost in these patients. Control patients with hypertension, hypercalciuria, and some of the diseases known to be associated with increased bone resorption did not exhibit hypercalcemia during thiazide administration. A hypercalcemic effect of thiazide diuretics, however, was also observed in three patients with malignant disease involving bone who were being treated for congestive heart failure.

These studies indicate the utility of the diagnostic use of thiazide diuretics in patients with symptoms suggesting hyperparathyroidism but in whom the chemical findings are intermittent or inconclusive.
CICC 2-06-322

GLUCOSE (Glu), INSULIN (IRI), CORTISOL (F) AND GROWTH HORMONE (HGH) DURING SATURATION DIVING. **J. Sode; E.T. Flynn; R. Bower and W.H. Spaur.** Naval Hospital, Bethesda and Navy Experimental Diving Unit, Washington, D.C.

Several investigators have reported decreases in blood Glu during NO₂ as well as HeO₂ (helium-oxygen) saturation diving. Although Glu remained within the normal range, the fall from 103 to 65 mg% reported in one study (Aerospace Med., 1971) represents a change of unexpected magnitude for conditioned healthy adults.

Since only limited information is available on hormone-substrate relationships in divers, we measured F by fluorometry, IRI and HGH by radioimmunoassay, and Glu, BUN (blood urea nitrogen) and electrolytes by autoanalyzer in ten subjects making a shallow HeO₂ saturation dive. Fasting blood samples were obtained just prior to the dive and after one full day's exposure at 75 feet. Whole blood was decompressed, and the serum separated and frozen until analyzed. At 75 feet, serum sodium (Na) was slightly lower ($p < .05$) but other parameters remained unchanged. All HGH values were under 5 ng/ml. Mean values \pm SEM (standard error of the mean) for serum Glu (mg%), IRI (mcU/ml) and F (mcg%) were: 103 ± 3.3 , 4.4 ± 0.3 , and 22.9 ± 2.0 respectively before the dive; and 102 ± 1.8 , 4.6 ± 0.4 and 23.2 ± 1.3 at 75 feet. Before the dive and at 75 feet, mean values for Glu and F were higher; for IRI and IRI/Glu, ratios were lower than those of fasting basal subjects.

This was consistent with the expected adaptive response to the stress of the experiment. The factors

contributing to the development of "hyperbaric hypoglycemia" and the role of immersion, depth and saturation exposure require further study.

CICC 2-06-324

LEFT RENAL VEIN (LRV) TO INFERIOR VENA CAVA (IVC) CORTISOL CONCENTRATION GRADIENT FOR PREOPERATIVE LOCALIZATION OF ADRENAL ADENOMA. **J. Sode; J.J. Sabol and D.A. Lee.** Naval Hospital, Bethesda.

Because percutaneous sampling of LRV blood is technically easier than adrenal vein catheterization, we evaluated LRV and IVC cortisol concentrations in nine euadrenal patients undergoing studies for suspected renovascular disease and in five patients with adrenocortical hyperfunction. In the euadrenal patients dexamethasone (DEX) suppressed LRV and IVC cortisol to under 5 mcg%. Mean cortisol concentrations (mcg%) under DEX in the five patients with adrenocortical hyperfunction were:

	No.	LRV	IVC
Bilateral hyperplasia	2	14.0	9.5
Left adrenal adenoma	3	47.3	29.3

Using data from the literature for renal blood flow and for distribution space and half life of cortisol, theoretical LRV to IVC cortisol gradients of 22% and 11% respectively were calculated for single and bilateral production sites. With the catheter proximal to the mouth of the adrenal vein, the observed gradients were higher, indicating preferential admixture of adrenal vein blood. For this reason, the gradient will not distinguish between bilateral hyperplasia and adenoma. On the other hand, in patients with accepted biochemical criteria for adenoma, a significant LRV to IVC cortisol gradient obtained on 8 mg/day of DEX is a reliable index of an autonomous left-sided cortisol source. The gradient is therefore useful for preoperative localization of adrenal adenoma when the adrenal veins proper cannot be cannulated.

CICC 2-06-324

WHOLE BODY RETENTION OF ORALLY ADMINISTERED 47-CALCIUM (Ca). **J. Sode; J.J. Sabol; W.M. Beckner; S.M. Fidler and J.J. Canary.** Naval Hospital, Bethesda and Georgetown University.

Ca balance techniques are too rigorous for clinical work. Yet, from the viewpoint of the body's Ca economy, the amount of Ca retained after oral ingestion is of paramount importance. For this reason we measured fractional retention of 47-Ca (47-CaRet) by whole body counter 7 days after an oral dose. In

many instances, 47-Ca absorption (CaAb) was also determined from kinetic analysis of plasma specific activity curves or from the ratio of oral over I.V. 47-CaRet. Patients were ambulatory and on a 0.8-1.0 g/day Ca diet. 47-CaRet (Mean \pm SD) as % dose in normal and diseased states was:

Normal subjects	(14)	38.4 \pm 5.1
Hyperparathyroidism	(21)	49.1 \pm 9.3
Acromegaly	(12)	52.6 \pm 10.1
Sarcoidosis	(14)	36.9 \pm 5.9
Idiopathic hypercalciuria	(5)	36.5 \pm 4.6
Malabsorption	(11)	24.4 \pm 3.5
Uremia	(9)	21.6 \pm 5.4
Hypoparathyroidism	(6)	27.6 \pm 3.5

47-CaRet reliably discriminated between different types of derangements of Ca metabolism and permitted objective evaluation of the efficacy of treatment. The test was helpful in distinguishing hyperparathyroidism from sarcoidosis and idiopathic hypercalciuria. Whereas CaAb is increased in all three conditions, 47-CaRet is usually normal in the latter two because of greater losses of absorbed radioactivity. The test is reproducible, requires small doses of tracer, and is suited for outpatient work since collection of urine and feces is not required.

CICC 2-06-325

MINERALOCORTICOID PRODUCTION IN NORMAL AND ACTH DEFICIENT SUBJECTS. R.L. Weinstein; B. Lai and T. Xenakis. Naval Hospital, Oakland.

Mineralocorticoid production was assessed by the excretory rates of tetrahydrodeoxycorticosterone (THDOC), tetrahydrocorticosterone (THB) and aldosterone (A) in five healthy adult volunteers during 5-day periods of normal (110 mEq), low (10 mEq) and high (210 mEq) sodium intake and after oral dexamethasone treatment (2 mg/day) for two days.

The mean level of THDOC (6.6 μ g/24 hr) and THB (189 μ g/24 hr) excretion on 110 mEq sodium showed no significant change during periods of sodium restriction or sodium loading. However, dexamethasone treatment resulted in a 60% (2.6 μ g/24 hr) and 88% (22.7 μ g/24 hr) decrease, respectively, in THDOC and THB excretion. Alternately, the mean level of A (13.6 μ g/24 hr) excretion on 110 mEq sodium increased 150% (34 μ g/24 hr) during sodium restriction and decreased 55% (6.0 μ g/24 hr) during sodium loading, while dexamethasone treatment resulted in no significant change (11.0 μ g/24 hr). Additionally, a 27-year-old male with isolated deficiency of pituitary ACTH was studied while receiving dexamethasone replacement. Urinary excretion of THB (16.1 μ g/24 hr) and

THDOC (4.8 μ g/24 hr) on 110 mEq sodium increased 100% (32.3 μ g/24 hr) and 90% (9.1 μ g/24 hr), respectively, during sodium restriction. Infusion of ACTH (40 μ over 8 hr/day) for two days now resulted in a marked increase in THB (101 μ g/24 hr) and THDOC (56 μ g/24 hr) excretion.

These studies demonstrate: (1) Production of THDOC and THB, unlike A, is primarily under ACTH control. (2) In the absence of ACTH, production of THDOC and THB increases during sodium restriction, suggesting further regulation by the renin-angiotensin system of these precursors of aldosterone.

MR005.20.01-0338A2HX

GONADAL AND PITUITARY INSENSITIVITY TO HUMAN CHORIONIC GONADOTROPIN (HCG) AND CLOMIPHENE STIMULATION IN KLINEFELTER'S SYNDROME. R.L. Weinstein; S.L. Kaplan and M.M. Grumbach. Naval Hospital, Oakland.

Gonadal and pituitary function were studied in six chromatin-positive (five - 47 XXY, one - 48 XXY) men with seminiferous tubule dysgenesis (STD), ages 16-26 years, and compared with normal adult males (NM). Mean levels of plasma testosterone (T) were low in STD (.28 μ g%) compared to NM (.50 μ g%). However, mean levels of plasma androstenedione (A) were similar in STD (.08 μ g%). Stimulation with HCG (5000 U daily x 4 days) resulted in a 50% increase in plasma T (.42 μ g%) in five out of six cases of STD, whereas a 100% increase occurred in plasma T (.99 μ g%) in NM. Again, the level of plasma A was similar in STD and NM (.13 μ g%) following HCG treatment, increasing 48% and 57%, respectively. Mean serum levels of follicle-stimulating hormone (FSH) (45 ng/ml) and luteinizing hormone (LH) (9 ng/ml) were markedly elevated in STD compared to NM (FSH 1.9 ng/ml and LH 1.5 ng/ml). Similarly, the FSH/LH ratio in STD (5.0) greatly exceeded this level in NM (1.3). Treatment with clomiphene in varying dosages (25 - 500 mg) showed no significant change in serum levels of FSH, LH, plasma T, or A in five out of six patients, while significant increases in FSH and LH (\geq 100%) and T (80-100%) occurred in all NM studied.

Administration of HCG and clomiphene in STD demonstrates the following: (1) Levels of plasma T were lower and less responsive to HCG administration compared to NM, indicating gonadal insensitivity. (2) Plasma A levels in STD were similar to those in NM before and after HCG treatment. (3) Elevated levels

of pituitary gonadotropins (FSH and LH) and low plasma T levels were unchanged after clomiphene administration in five out of six STD compared to NM, indicating pituitary insensitivity.
MR005.20.01-0345A2GX

PITUITARY-TESTICULAR RESPONSIVENESS IN HYPOGONADOTROPIC HYPOGONADISM. I. BIOCHEMICAL OBSERVATIONS. R.L. Weinstein and R.E. Reitz. Naval Hospital, Oakland.

Isolated deficiency of pituitary FSH and LH was demonstrated in five 46.XY males, 22-36 years of age, with and without anosmia. Serum FSH was undetectable (< 1 mIU/ml) in all gonadotropin deficient subjects (adult males, 6.2 ± 2.3 SD mIU/ml), while serum LH was detectable (1.6 mIU/ml) in only one subject (adult males, 7.9 ± 2.6 , SD mIU/ml). Clomiphene citrate (50-200 mg/day \times 12 weeks) caused no rise in serum FSH, LH or plasma testosterone (T). While plasma T was markedly low (.03 μ g%), plasma 17-ketosteroids, androstenedione (A) .08 μ g%, and dehydroepiandrosterone (D) .38 μ g%, were similar to levels of A (.10 μ g%), and D (.53 μ g%), in adult males.

Conclusions: (1) Measurement of serum FSH and LH clearly separated hypogonadotropic from normal adult males. (2) Undetectable or low FSH and LH were unresponsive to clomiphene therapy.
MR005.20.01-0193A2GX

PITUITARY-TESTICULAR RESPONSIVENESS IN HYPOGONADOTROPIC HYPOGONADISM. II. EFFECT OF FSH AND LH PREPARATIONS ON TESTICULAR FUNCTION AND STRUCTURE. R.L. Weinstein and R.E. Reitz. Naval Hospital, Oakland.

Isolated deficiency of FSH and LH has been documented in five adult males. Undetectable or low levels of FSH and LH were present in all subjects, and no response to clomiphene was observed with acute or chronic administration. After four weeks of human chorionic gonadotropin (HCG) 5000 U, 3 x/wk), plasma testosterone (T) increased from 0.03 μ g% to 0.60 μ g% (adult males, 0.63 μ g%). During nine months of HCG administration, increasing masculinization was observed. Addition of Pergonal (PMG) (containing both FSH and LH) caused an increase in spermatogenesis observed in testicular biopsy specimens and the presence of sperm in the ejaculate, although no significant increase in levels of plasma T, 0.69 μ g%, was observed. Fertility was established in one subject.

Conclusions: (1) Adult levels of plasma T after HCG confirm Leydig cell responsiveness in these

subjects. (2) Increased spermatogenesis was observed after treatment with HCG and PMG. (3) Addition of PMG to HCG treatment failed to further increase levels of plasma T.
MR005.20.01-0193A2GX

STARVATION AND LIVER GLUCONEOGENESIS (GNG). H.V. Werner. Naval Hospital, Oakland.

GNG in Mammalia *in vivo* is thought to be increased during starvation. This has been explained by an increased activity of the liver enzymes unique to GNG; yet, the activity of one of these three enzymes, fructose-1,6-diphosphatase, is unchanged. Isolated parenchymal cells from rat liver were prepared from fed, from 24-hour fasted and from fed-glycogen depleted (by anaerobic perfusion) rats, and rates of glucose production were measured enzymatically. Precursors (10 mM) and rates of GNG (μ moles Gm⁻¹ min⁻¹, mean \pm SD) were:

SUBSTRATE	FED-GLYCOGEN		
	FASTED	DEPLETED	FED
.....	.10 \pm .02 (10)	.13 \pm .05 (4)
Lact	.67 \pm .06 (7)	.40 \pm .11 (4)	.61 \pm .18 (2)
Pyr	.54 \pm .08 (7)	.45 \pm .10 (4)	.73 \pm .24 (2)
Fruc	2.41 \pm .41 (5)	2.42 \pm .28 (4)	2.74 \pm .29 (2)
Sorb	1.47 \pm .17 (8)	1.42 \pm .23 (4)	1.72 \pm .07 (2)
Dihyd	1.86 \pm .09 (4)	1.66 \pm .22 (4)	2.03 \pm .28 (2)
Glyc	.53 \pm .05 (8)	.52 \pm .13 (4)	.54 \pm .11 (2)
Ala	.30 \pm .03 (5)	.25 \pm .06 (3)

The data indicate that rat liver parenchymal cells when presented with a 10 mM concentration of precursor, synthesize glucose in the fed state, as well as after fasting. Specific enzyme levels, therefore, are not rate-limiting for GNG; rather substrate concentration is a more crucial variable in determining these rates in liver parenchymal cells.

MR005.20.01-0383A2GH

CONTROL OF GLYCEROL METABOLISM IN LIVER. H.V. Werner. Naval Hospital, Oakland.

An obvious link between carbohydrate and lipid metabolism in man during stress is glycerol. It is liberated during lipolysis (increased in starvation and exercise) and then synthesized by liver into glucose for peripheral utilization, e.g., muscle. Sorbitol also is metabolized only by liver. Their metabolism was compared to determine limiting steps of glycerol metabolism in isolated liver parenchymal cells from

fasted rats. Each pathway contains an (nicotinamide adenine dinucleotide) NAD-linked oxidation: (a) sorbitol \rightarrow fructose; (b) after an initial phosphorylation of glycerol to α -glycerophosphate (α -GP), α -GP is oxidized to dihydroxyacetone phosphate (DHAP). These oxidation steps are rate limiting since: (1) the rate of removal of fructose (μ moles/gm/min, mean \pm SD), $3.75 \pm .21$, is much greater than sorbitol, $1.64 \pm .20$; and (2) when cells are exposed to glycerol, α -GP accumulates to high levels, $11.9 \pm .3$ μ moles/gm (normal 0.17), and DHAP is unchanged.

When sorbitol and glycerol were added together, competition was evident: (a) Removal rates of each decreased by 50-75%, and (b) glucose and lactate production rates were not additive. Addition of pyruvate (cytoplasmic acceptor of reducing equivalents) to sorbitol-containing medium indicated that the initial oxidation of sorbitol was limiting since rates of GNG and removal of sorbitol approached those of fructose. Metabolism of glycerol in the presence of pyruvate, in contrast, was not increased, as judged by removal rates or GNG. This indicated that glycerol and pyruvate do not share a common cytoplasmic NAD pool; thus, the rate-limiting step in glycerol metabolism is of mitochondrial origin, viz, the rate of transfer of reducing equivalents.

MR005.20.01-0383A2GH

GLUCOSE AND FREE FATTY ACID (FFA) – KETONE INTERACTIONS AFTER EXERCISE. H.V. Werner and R.E. Reitz. Naval Hospital, Oakland.

An abnormal tolerance to ingested glucose (GTT) in the period following exercise has been reported and explained as inhibition by a concomitant elevation of FFA and ketones, i.e., post-exercise ketosis. To test this hypothesis, nine male volunteers were exercised by running for 90 minutes, and after a 30-minute rest, tested for glucose tolerance.

Glucose and insulin (IRI) levels did not change during exercise, while growth hormone (HGH), glycerol, cortisol, FFA and ketones became elevated. After exercise ceased, FFA and ketones further increased, reaching a peak by time 0 (1.58 ± 0.29 and 0.58 ± 0.25 mM, mean \pm SEM). During the subsequent 120 minutes FFA and ketones were not significantly changed. When a GTT was performed, however, they returned to baseline range in 30-60 minutes. In contrast, glycerol, HGH and cortisol declined after exercise irrespective of glucose intake, and reached baseline values at 30, 60 and 120 minutes, respectively. Since net lipolysis ceased 60 minutes (time 15-30 minutes) post-exercise, i.e., glycerol returned to baseline

levels, the data indicate a striking inhibition of FFA and ketone utilization following exercise only when glucose was not given. Oral (6) and intravenous (3) GTTs performed in the post-exercise period were normal despite elevated levels of so-called anti-insulin hormones (HGH and cortisol) and metabolites (FFA and ketones). No competition between glucose and FFA-ketones as substrates ("Randle effect") was detected; instead, a synergistic effect of each metabolite was seen on the utilization of the other.

MR005.20.01-0378A2GH

FATTY ACID EFFECTS ON GLUCONEOGENESIS (GNG) IN ISOLATED RAT LIVER PARENCHYMAL CELLS. H.V. Werner. Naval Hospital, Oakland.

Elevated levels of fatty acids are thought to stimulate GNG by providing reducing equivalents via their increased oxidation. Provision of glucose precursors and fatty acids, or their analogues, might enhance endurance, e.g., during exercise in which glycogen depletion heralds exhaustion.

Precursors were studied and their baseline rates of glucose production (μ moles/gm/min, mean \pm SD) by isolated parenchymal liver cells of fasted rats were determined: pyruvate, $0.56 \pm .09$ (5), lactate, $0.72 \pm .07$ (5), sorbitol, $1.45 \pm .10$ (3) and glycerol, $0.55 \pm .05$ (6). GNG from pyruvate was stimulated by the fatty acids C₈ through C₁₈ ($p < .05$); with sorbitol, glycerol or lactate, the acids C₈ through C₁₄ were markedly inhibitory ($p < .005$), while C₁₆₋₁₈ were without effect. Further studies with decanoate (C₁₀) and oleate (C₁₈) indicated that the enhanced GNG from pyruvate was due not to increased removal from the medium, but to a shift in flux toward glucose, probably by greater availability of reducing equivalents from increased (by 50%) fatty acid oxidation. The lower GNG rates from sorbitol, glycerol or lactate in the presence of C₁₀, in contrast, were accounted for completely by decreased substrate utilization. Since the metabolism of C₁₀ and these substrates each requires nicotinamide adenine dinucleotide (NAD), competition for the oxidation of generated NADH by the respiratory chain was evident.

It is concluded that (1) fatty acid chain length and type of precursor are important determinants of gluconeogenic rates, and (2) medium chain fatty acids compete effectively with lactate, sorbitol or glycerol for oxidation in isolated rat liver parenchymal cells.

MR005.20.01-083A2GH

GLUCOSE-ATP-6-PHOSPHOTRANSFERASES IN ISOLATED RAT LIVER PARENCHYMAL CELLS. H.V. Werner. Naval Hospital, Oakland.

Whole liver homogenate contains at least four enzymes which phosphorylate glucose, the initial step in its utilization. Three of these are hexokinases, which have low K_m (10^{-4} to 10^{-6} M) and are unaffected by starvation; the fourth, glucokinase, $K_m = 10^{-2}$ M, is markedly lowered during fasting and probably accounts for the lowered utilization of glucose by liver during starvation. Controversy exists as to whether hexokinase is located in the parenchymal cell, per se, and can contribute to its utilization of glucose.

Cells were isolated by differential centrifugation after perfusion of the liver with collagenase-hyaluronidase. Enzyme assay (photometer) data were confirmed and elucidated by gel electrophoretic and column chromatographic methods. Data are expressed as units per gram liver (mean \pm SD). In fed animals, glucokinase in cells ($1.50 \pm .20$) was insignificantly different from whole liver, $1.29 \pm .18$ (7). After fasting 24 hours (4) glucokinase in cells decreased 64%, reached nadir after three days (5), and was not further changed even after seven days (4). All three isoenzymes of hexokinase were found in parenchymal cells ($.23 \pm .05$) and their level was significantly lower ($p < .005$) than whole liver ($.33 \pm .05$) in the fed state. These values were unchanged by fasting, but in all periods up to eight days, parenchymal cell hexokinase was significantly lower than in whole liver ($p < .02$).

Conclusions: (a) Isolated rat liver parenchymal cells contain all three low K_m hexokinases as shown by photometry, electrophoresis and chromatography, but (b) these hexokinases are located primarily in non-parenchymal cells of the rat liver.

MR005.20.01-0390A2GH

GASTROENTEROLOGY

DIAGNOSIS AND PRESURGICAL EVALUATION OF BILIARY AND PANCREATIC DISORDERS UTILIZING A FIBER-JEJUNOSCOPE. E.L. Burke. Naval Hospital, Portsmouth, Va.

Evaluation of pancreatic and biliary ductal systems particularly in the presence of jaundice is presently available only by operative or immediately preoperative procedures. This project is designed to provide routine preoperative evaluations of these disorders

using the technique of cannulation of the pancreatic and biliary tree utilizing peroral endoscopy.
CICC 2-08-508

EVALUATION OF INFERIOR ESOPHAGEAL SPHINCTER COMPETENCE BY ESOPHAGOSCOPY. E.L. Burke. Naval Hospital, Portsmouth, Va.

Extensive clinical experience with esophagoscopy suggests that in cases with strong history compatible with esophageal reflux, the sphincter remains persistently open during endoscopy with the flexible instrument. This study is designed to quantitate the "open time" of the sphincter in various clinical situations by use of endoscopic cinephotography and through the measurement of sphincter strength by esophageal manometry.

CICC 2-08-514

COMBINED ASCITIC FLUID REINFUSION AND INTRAVENOUS ETHACRYNIC ACID IN TREATMENT OF ASCITES. E.L. Burke. Naval Hospital, Portsmouth, Va.

Experience today has shown that with appropriate technique urine flow rates of 1500 cc per hour can be obtained, making it possible to remove massive amounts of ascites in a short time, leaving the patient in good metabolic balance with a higher serum albumin and sodium than before the procedure. The procedure has proven safe in hepatic coma. It is not a procedure to be used in the absence of a skilled team.

MR041.20.01-0330A2GX

CORRELATION OF PORTAL HEMODYNAMIC ABNORMALITIES WITH SEVERITY OF CHRONIC LIVER DISEASE. D.O. Castell; R.L. Farrell and O.T. Nebel. Naval Hospital, Philadelphia.

Recent studies have indicated that radioactive Xenon gas can be utilized as a functional test of the portal circulatory dynamics by monitoring the time for rectally-administered Xenon to appear in the heart blood. The present studies were undertaken to further delineate the relationship of the Xenon "rectum-to-heart time" to the portal flow. Preliminary basic studies will be performed in dogs in whom the portal pressure and flow will be measured directly during laparotomy. Following the surgical creation of portal hypertension, portacaval anastomosis, and occlusion, and occlusion of the portacaval anastomosis, Xenon studies will be repeated. Comparison will be made between the measured circulation time and the portal hemodynamics

measured directly in these animals. An attempt will be made to utilize this basic experimental information to further apply the Xenon circulation time as a functional test of liver portal hemodynamics in patients with hepatic disease.

This is a new work unit and studies are being initiated at the present time.

CICC 2-05-601

ILEAL REFLUX AFTER GASTRIC ALKALINIZATION. D.O. Castell; R.A. Love and M. Ramer. Naval Hospital, Philadelphia.

Recent physiological studies have indicated that the gastrointestinal hormone gastrin causes marked relaxation of the human ileocecal sphincter. The present investigation was undertaken to evaluate the relationship of stimulation of endogenous gastrin release by gastric alkalization, to the ability to reflux barium into the terminal ileum during barium enema examination. The potential usefulness of this procedure would be to increase the diagnostic capability of the barium enema examination in the radiographic diagnosis of disease of the terminal ileum.

The studies are being performed in a randomized blinded manner, with the diagnostic radiologist being completely unaware of whether the patient is receiving placebo or gastrin stimulation. Films will be interpreted blindly using objective evidence of ileal reflux as the end point. An attempt will be made to study consecutive patients seen in the X-ray department of this hospital who do not show terminal ileal reflux during routine barium enema examination.

Initial studies indicate a real potential for gastrin stimulation in promoting reflux of barium into the terminal ileum.

CICC 2-05-606

EXAMINATION OF THE DESCENDING COLON WITH THE FIBEROPTIC COLONOSCOPE. A.R. Chappelka; O.T. Nebel and D.O. Castell. Naval Hospital, Philadelphia.

Seventy-one patients with large bowel symptomatology have been examined by means of a recently developed fiberoptic colonoscope. A variety of lesions have been visualized and biopsied including: polyps (16), colitis (7), carcinomas (3), and diverticulosis (1). In forty-six patients no abnormality could be found. A report concerning the clinical effectiveness of this procedure was presented at the 1971 Boston Naval Hospital Symposium.

Current studies are being conducted in cooperation with NAMRU-3 and involve the colonoscopic evaluation of schistosomal colonic disease. Previous publications from NAMRU-3 have characterized the colonic lesion in this disease. They have also documented radiographic resolution of these polypoid lesions with medical therapy. However, despite this response to medical treatment, colectomy still remains the most widely-used treatment for this complication. Since there is some question as to the character of the post-treatment mucosa, we plan to evaluate endoscopically the pre- and post-treatment colonic mucosa of patients with schistosomal polyposis. It is hoped that this information will lead to a more rational approach to therapy.

MR041.20.01-0348A2GX

EVALUATION OF ACUTE DIARRHEAL STATES IN THE MILITARY POPULATION. A.R. Chappelka and D.O. Castell. Naval Hospital, Philadelphia.

Nonspecific acute diarrhea is one of the major problems in medical absenteeism in the armed forces. This is true not only in the combat zones but in the military population at large. The cause and mechanisms of nonspecific diarrhea are not well understood and numerous factors have been implicated, including viral and bacterial invasion, enterotoxins, and alterations of host defense mechanisms.

For the past year the Gastroenterology Branch of the Philadelphia Naval Hospital and Thomas Jefferson University have been involved in a joint project aimed at monitoring the changes in total microflora during acute and chronic diarrheas of unknown etiology. Studies utilizing the most sophisticated protocols available in both anaerobic and aerobic bacteriology have been employed in the sampling of these populations both from the small bowel and stool. Simultaneously aspirate has been studied for immunologic host response. Approximately 50 cases have been evaluated in detail in order to elucidate those shifts in microflora and immunoglobulin which characterize the diarrheal state. Matched control populations have been studied longitudinally to delineate normal indigenous microflora.

MR041.20.01-1372A2GJ

EVALUATION OF BLOOD VOLUME CHANGES AND SEPSIS INDUCED BY PARENTERAL HYPERALIMENTATIONS. D.D. Foote; M.J. Attkiss; W.C. Johnson and R.L. Mullin. Naval Hospital, Boston.

Intravenous hyperalimentation has been a valuable tool in the surgeons' "armamentarium." Possible deleterious side effects are hypophosphatemia, changes in blood volume and septicemia. Data related to these side effects will be compiled. Hypophosphatemia associated with hyperalimentation was reported in NEJM 285763 1971 and will not be included in this investigation. However, changes in blood volume and the incidence of sepsis when using Silicone Medicath catheters is currently under investigation.

CICC 2-02-108

GASTRIC SECRETORY PATTERNS IN PATIENTS WITH HIATAL HERNIA AND CONCOMITANT PEPTIC ULCER DISEASE. M.F. Fornes. Naval Hospital, San Diego.

Patients with esophageal hiatus hernia and duodenal or gastric ulcer disease will be included in this study. The presence or absence of reflux will be determined by endoscopy, biopsy and clinical symptoms. Reflux will be further substantiated by intra-esophageal pH measurements pre- and post-acid infusion. Each patient will also undergo gastric analysis.

It is hoped that the above studies will shed more conclusive light on the role of hydrogen ion in the etiology of reflux esophagitis. If a patient with a gastric ulcer and hiatal hernia, who is also hypochlorhydric, does not get symptomatic esophagitis, we have established that the degree of hydrogen ion concentration plays an important part in the generation of esophagitis. If the above relationship can be established, we might also add confirmation to the findings of others that gastrin increases local excitatory state (LES) pressure. The hypochlorhydric state might lead to increased gastrin production, increased gastrin levels might lead to increased LES pressure and this, in turn, would tend to protect against reflux in these patients.

CICC 2-16-420

CLINICAL EVALUATION OF THE INAPPARENT HIATUS HERNIA. R.D. Gaskins; M.F. Fornes; R.B. Johnson and W.M. Lukash. Naval Hospital, Bethesda.

We have recently completed a 100-patient clinical study in an effort to substantiate the presence of a hiatus hernia when the symptoms of pyrosis, dysphagia or chest pain were presented.

In this study, gastrointestinal X-rays, endoscopy, gastric and esophageal biopsies and acid Bernstein drip were performed and evaluated by three different investigators. The study revealed the presence of a hiatus hernia in 81% while it was evident by X-ray studies in only 44%. Esophageal reflux was seen in 40% and esophagitis in 54%. Mucosal biopsy, however, showed inflammation in only 21% of the patients tested. The Bernstein drip was positive in 41%. It appeared that though the symptoms were most likely due to disease in the lower esophagus, the tremendous overlap in the subjective interpretation of these clinical tests by both physicians and patients suggests the need for a more objective diagnostic approach.

Recent evidence would indicate that esophageal manometric measurements of the lower esophageal sphincter are more objectively related to the hiatus hernia symptom complex.

CICC 2-06-303

EVALUATION OF INTESTINAL ABSORPTION IN VIRAL HEPATITIS. R.H. Higgs and A.R. Chappelka. Naval Hospital, Philadelphia.

Viral hepatitis is a significant disease among personnel in the armed forces. We intend to determine if malabsorption occurs in viral hepatitis, since an altered therapy might facilitate earlier return to active duty.

The parameters being used are (1) serum carotene, (2) D-xylose excretion, and (3) oral fat tolerance test.

The project has just commenced and no valid conclusions can be drawn at this time.

CICC 2-05-605

VIVONEX IN PREOPERATIVE BOWEL PREPARATION. W.C. Johnson and D.D. Foote. Naval Hospital, Boston.

Analysis of data on ten patients who were given Vivonex in preparation for colonic surgery revealed a 20% incidence of wound infection. Benefits of the Vivonex were that the patient could maintain a daily 2000 calorie intake up to the day of surgery. Colonic residue was minimal and not troublesome. Retrospective analysis of 20 patients undergoing colonic surgery with a conventional bowel preparation revealed a 25% incidence of wound infection. Since Vivonex-treated patients fared no worse and maybe better than the control group, a prospective randomized study was initiated in November 1971.

CICC 2-02-103

SERUM MONOAMINE OXIDASE: AN INDEX OF HEPATIC FIBROSIS. J.P. Kirchner and D.O. Castell. Naval Hospital, Philadelphia.

Human serum contains a soluble monoamine oxidase (MAO) which deaminates a variety of monoamines. We have studied MAO values in normal subjects and in patients with acute and chronic liver disease. Forty-two normal subjects with an age range of 18 to 75 years had a mean value of 33.3 ± 1.2 (± 1 SE) units. Thirty-five patients with clinical and histologic evidence of hepatic cirrhosis had a mean MAO level of 44.8 ± 2.9 units, which was significantly greater ($p < 0.001$) than the normal level. By contrast, 27 patients with acute hepatitis had a mean MAO level of 31.7 ± 1.4 units. This was not significantly different ($p > 0.30$) from the mean normal MAO but was significantly less ($p < 0.001$) than the mean MAO for the cirrhotic patients. In addition, there was no positive correlation between serum MAO levels and standard hepatic function tests (transaminases, alkaline phosphatase, bilirubin, or prothrombin time) in the patients with either acute or chronic liver disease. During the production of experimental hepatic cirrhosis with carbon tetrachloride in rabbits serum, MAO values have more than doubled when compared with MAO and preinjection values obtained in control rabbits.

Conclusion: Serum MAO levels are elevated in liver disease only when hepatic fibrosis is present, and are not related to abnormalities of other liver enzymes. This unique enzyme may be a valuable early clue to the development of cirrhosis in man.
MR041.20.01-0320A2GX

DIAGNOSTIC HISTOLOGIC CRITERIA IN INFLAMMATORY BOWEL DISEASE IN MILITARY PERSONNEL. W.M. Lukash; R.B. Johnson; R.D. Gaskins and L.G. Dixon. Naval Hospital, Bethesda.

A common problem in digestive diseases involving members of the armed forces is that of nonspecific ulcerative proctitis. Although this is a self-limited disease in a majority of these patients, some 15-20% develop progressive involvement to the extent that they have ulcerative colitis universalis. In addition, the endoscopic diagnosis in the rectum is difficult at times to differentiate from that of granulomatous proctitis. We plan to compare findings on rectal biopsy both by light and electron microscopy. By using colonoscopy and obtaining a biopsy in both the area of inflammation and in normal mucosa proximal to the rectum, more differentiating histologic findings might be established. This may be useful in predicting what patients will progress to more extensive disease and should also

provide more objective clues to the overall spectrum of this condition.
MR041.20.01-0349A2HX

EVALUATION OF UPPER GASTROINTESTINAL (UGI) BLEEDING IN MILITARY PERSONNEL UTILIZING DUODENOSCOPY. O.T. Nebel and A.R. Chappelka. Naval Hospital, Philadelphia.

We have utilized a vigorous diagnostic approach (VDA) in the evaluation of 25 patients with acute UGI bleeding. A pathologic lesion to account for the bleeding was found in all patients. These lesions were diagnosed by the technique of radiography (3), esophagoscopy (4), gastroscopy (8), and duodenoscopy (5). By contrast, in a group of eight patients with only a history of UGI bleeding, a pathologic lesion was found in only four cases. The lesions were diagnosed by esophagoscopy (1) and duodenoscopy (3).

These data support previous observations of the importance and efficacy of the VDA in the evaluation of UGI bleeding, and indicate that duodenoscopy may be an important procedure in this approach. In addition duodenoscopy has been performed in 30 patients who presented with UGI symptomatology, and who were found on UGI X-ray to have a deformed duodenal bulb. Six patients were thought to have active ulceration radiographically but only three active ulcers were confirmed on duodenoscopy. However, three radiographically unrecognized ulcerations and three severe duodenal erosions were diagnosed by duodenoscopy. In ten patients the duodenum appeared normal.

Because of the small number of cases no definite conclusions can be drawn. Preliminary data suggest that duodenoscopy with the Olympus JG-B is a simple effective technique which may be of substantial value in the evaluation of patients with UGI bleeding and symptomatic duodenal bulb deformity.
CICC 2-05-603

PHYSIOLOGIC CONTROLS OF LOWER ESOPHAGEAL SPHINCTER PRESSURE. O.T. Nebel, R.L. Farrell and D.O. Castell. Naval Hospital, Philadelphia.

The lower esophageal sphincter (LES) has been shown previously in this laboratory to respond to various hormones and drugs. We have further evaluated the effect of basic foods and the cholinergic agent Urecholine on this sphincter. All studies were done using an infused open-tipped recording system. The majority of physiologic studies were performed in healthy male volunteer subjects. Basic food studies indicate that: consistent increases in LES pressure

occur after protein ingestion, no change in pressure occurs after carbohydrate ingestion, and marked decreases in sphincter pressure are produced by fat ingestion. The ingestion of a combined protein-fat meal results in decreased sphincter pressure, although less marked than that observed following the fat meal alone. The mechanism of this effect appears to be the inhibition of the normal physiologic stimulation of gastrin on the LES, probably through the release of a duodenal hormone.

Marked increases in LES pressure occur in both normal subjects and subjects with incompetent LES following the injection of 5 mg of Urecholine subcutaneously. In addition, oral Urecholine (25 mg) produced increases in LES pressure in patients with an incompetent sphincter. LES pressure rose to the range found in normal subjects. These studies have suggested a potential clinical role for this drug in the treatment of gastroesophageal reflux. A double-blind controlled clinical trial is currently underway at this hospital.
MR041.20.01-0321A2GX

HYPERALIMENTATION. R.E. Pries and G.A. Ulch. Naval Hospital, Great Lakes.

Sufficient equipment and nutrient have now been obtained through this project to establish a formal format for this program. A protocol has been distributed to ward medical officers and several requests for parenteral hyperalimentation have been received. They are now being processed.
CICC 2-13-001

DIAGNOSTIC ACCURACY OF FIBEROPTIC DUODENOSCOPY IN EVALUATING UPPER GASTROINTESTINAL HEMORRHAGE. J.Q. Stauffer. Naval Hospital, Great Lakes.

Rapid and accurate diagnosis of acute upper gastrointestinal hemorrhage is essential in the management of these patients. Upper gastrointestinal X-rays, and fiberoptic esophagoscopy and gastroscopy are now standard procedures employed to establish the site of bleeding. Recently, fiberoptic duodenoscopy has been utilized routinely and has been reported to offer greater accuracy than X-ray studies in localizing bleeding from the duodenum.

The Olympus GIF No. 180-1 duodenoscope has been ordered, and this question will be addressed when the instrument becomes available. On a prospective basis all patients with upper gastrointestinal bleeding will be evaluated by fiberoptic endoscopy and X-ray

studies; the diagnostic accuracy of each method will be compared. The feasibility of routine duodenoscopy in this group of patients will be evaluated.
CICC 2-13-005

PATHOPHYSIOLOGY OF CALCIUM OXALATE RENAL CALCULI IN PATIENTS WITH REGIONAL ENTERITIS. J.Q. Stauffer. Naval Hospital, Great Lakes.

Patients with granulomatous bowel disease are known to have an increased incidence of calcium oxalate renal calculi. It has been proposed that this is related to abnormal bile salt metabolism which is known to occur in these patients. When the enterohepatic circulation of bile salts is interrupted in the diseased state, there is an increased reabsorption of glycine from the colon as the result of bacterial deconjugation of the bile salts. The glycine is metabolized in the liver and excreted in the urine as calcium oxalate.

A patient who has had resection of the terminal ileum because of complications of regional enteritis has been evaluated. On a control diet of 2150 calories containing 60 g fat and 750 mg of calcium, she was shown to have steatorrhea, malabsorption of fat-soluble vitamins and a choleretic enteropathy reversible with administration of cholestyramine. During a control period the patient was found to have an increased urinary excretion of calcium oxalate of 106 mg/24 hrs (Normal 9-39 mg/24 hrs). When cholestyramine (which is known to bind bile salts) was given, the urinary oxalate excretion decreased to 23 mg/24 hrs.

This data supports the hypothesis that deconjugation of bile salts with reabsorption of glycine from the colon leads to increased urinary excretion of calcium oxalate. Reversal of the hyperoxaluria with oral cholestyramine has therapeutic implications in the prevention of renal calculi formation in patients with a diseased or absent terminal ileum.
CICC 2-13-010

HEMATOLOGY

STUDY OF COAGULATION SYSTEM IN PATIENTS WITH CHRONIC HYPOXIA. R.A. Burningham and J.E. Engeler, Jr. Naval Hospital, Philadelphia.

A severe bleeding diathesis was recently noted and studied at this hospital in a patient with chronic hypoxia secondary to chronic obstructive lung disease. The clinical course and laboratory data indicated a severe disseminated intravascular coagulopathy (DIC). None of the usual causes for DIC could be found. The present study was designed to investigate coagulation mechanisms in patients with chronic hypoxia.

All patients admitted to the Medical Service with known cardiopulmonary disease and an arterial PO₂ of less than 88 mm Hg at rest will be studied. The following tests will be performed: complete blood count, platelet count, bleeding time, prothrombin time, non-activated partial thromboplastin time, Stypven time, thrombin time, fibrinogen level, serial protamine sulfate dilution test, fibrin degradation products, platelet retention test, and platelet aggregation. At least 20 patients will be studied and appropriate controls will be established.

CICC 2-05-608

HISTOCHEMICAL DETERMINATION OF ENZY-MATIC ACTIVITY IN BLOOD DISORDERS. R.A. Burningham and J.E. Engeler, Jr. Naval Hospital, Philadelphia.

Burningham and Yunis found increased levels of inactive phosphorylase activity in human leukemic leucocytes from patients with untreated chronic myelocytic leukemia. On the basis of these data, an explanation for low glycogen levels in leukemic leukocytes was proposed. A histochemical method for determining phosphorylase content of leucocytes was developed by Wulff and Soressen (*Acta Haemat* 35:304-310, 1966). Since phosphorylase had not been investigated to any extent in other types of blood dyscrasias, the study was established to survey the patterns of phosphorylase activity in acute and chronic leukemias, myelofibrosis, polycythemia rubra vera, leukemoid reaction, and preleukemic states such as refractive normoblastic anemias, sideroblastic anemias, chronic idiopathic neutropenias and thrombocytopenias. Phosphorylase score was determined on normal control marrows with a range of 92 to 200.

A total of 20 determinations were made on 12 patients as follows: Acute myeloblastic leukemia (AML) (2), acute lymphoblastic leukemia (3), malignant

lymphoma (2), refractive normoblastic anemia (non-sideroblastic) (2), leukemoid reaction (1), and anemia of undetermined etiology (2). Phosphorylase score was within the normal range for all determinations except for one AML patient with a score of 40 and 68 respectively, in two determinations. After a complete remission of short duration, this patient suffered a relapse with manifest clinical, morphologic and karyotype criteria for chronic myelocytic leukemia. Further studies are being conducted to establish a definite pattern.
MR041.20.01-0125A2GX

CARE OF COMBAT CASUALTIES — BLOOD PRESERVATION — RED CELL MEMBRANES. R.A. Burningham. Naval Hospital, Philadelphia.

Since a number of excellent studies were published while this study was underway, the experimental design was modified to investigate hemolytic mechanisms, red cell membranes, and coagulopathies in patients with hypertensive vascular disease. The so-called "fragmentation syndrome" and disseminated intravascular coagulation have been described in patients with malignant hypertension. Screening studies consisting of a complete blood count, reticulocyte count, Coombs' test, prothrombin time (PT), thrombin time (TT), non-activated partial thromboplastin time (NPTT), platelet count (PC), Stypven clotting time (SCT), fibrinogen level, and the presence of fibrin or fibrinogen degradation products, were performed on patients admitted to the Medical Service with the diagnosis of hypertensive vascular disease. All patients had diastolic blood pressures greater than 100 mm Hg. The liver function studies and the blood urea nitrogen were normal. There was no evidence of infection or underlying blood dyscrasias. Thirty-eight separate screening studies were performed on 32 patients. Seven patients were found to have a significant reticulocytosis without anemia in the majority of cases. The red blood cell morphology was abnormal, but nonspecific. Two patients showed definite evidence of "fragmentation syndrome." The presence of the fibrin degradation products was demonstrated in one patient on repeated assays with otherwise normal coagulation screening studies. Further elucidation of the mechanisms involved is currently being undertaken.

MR041.20.01-0126A2GX

LYSOZYME ACTIVITY IN VARIOUS BIOMEDICAL DISORDERS. R.A. Burningham and J.E. Engeler, Jr. Naval Hospital, Philadelphia.

Serum lysozyme levels have been reported to be elevated in: certain myeloproliferative disorders such as acute monoblastic leukemia, acute myeloblastic leukemia, chronic myelocytic leukemia (CML); tuberculosis and sarcoidosis; and renal disease. The purpose of this study was to determine the serum lysozyme activity in a wide variety of hematologic and non-hematologic conditions, to determine the specificity of lysozyme levels in myeloproliferative disorders as compared to leukocytosis secondary to infection or other disorders causing a reactive leukocytosis, and to correlate lysozyme levels with response to therapy and prognosis of the specific disease state.

Serum samples were collected from patients referred to the Hematology/Oncology Branch. The lysozyme activity was determined by a modified turbidimetric method of Smolele and Hartsell (J Bacteriol 58:731, 1949). A total of 259 determinations have been made. Ninety have been found to be above the usual normal range of 2-10 ng/ml. In addition to the expected elevation in the myeloproliferative state and patients with renal disease and azotemia, five of 17 patients with metastatic carcinoma had significant elevation of the lysozyme level. In these patients there was no correlation with peripheral leukocyte count or azotemia. Two patients with refractive normoblastic anemia and probable preleukemic state had elevated levels. Further studies are being conducted especially in regard to leukocyte kinetics as recently reported by Hansen and Korte (Br J Haematol 21:261, 1971).

MR041.20.01-0191A2GX

FACTOR VIII LEVELS IN MENORRHAGIA. E.F. Cantow and J.E. Kostinas. Naval Hospital, Portsmouth, Va.

Von Willebrand's disease in the female may be manifested as recurrent unexplained menorrhagia. A study is underway utilizing Factor VIII levels as a screening procedure. Since the incidence rate of von Willebrand's disease in a given population is unknown, a large sample of patients presenting to this facility with unexplained menorrhagia will be screened. Low Factor VIII levels will be confirmed by repeat examination and those patients having two levels below 60% will be further evaluated historically and with a complete bleeding survey.

If the incidence of von Willebrand's disease is high in patients with menorrhagia, it is possible that they may segregate into a group which can be more easily

identified than at present. This segregation would be of considerable interest to the gynecologist in the management of these patients. In addition, an incidence figure for a selected population (female, menstruating) would be established.

CICC 2-08-510

STROMAL AND CELLULAR FACTORS IN HEMOPOIETIC FAILURE. J.L. Curry and A. Ruder. Naval Medical Research Institute (NMRI), Bethesda.

Viable hemopoietic grafts required in casualties with marrow failure caused by malarial chemoprophylaxis, radiation accidents, or nuclear weapons, require both regenerative stem cells and hemic inductive microenvironments (HIM). Methods of independently assaying both factors in human marrow are necessary to identify the lesion in cases of marrow failure and to develop rational therapy. Heretofore it has been impossible to study the relationship between stem cells and HIM in humans because of the lack of an *in vitro* system of hemopoiesis.

For the past year, this laboratory has been developing such a system in order to assay both the cellular and stromal factors in human marrow failure. The system currently used consists of an organ culture preparation of marrow biopsy material, suspended on a porous filter floating on the surface of a culture medium. In this system it has been possible to demonstrate hemopoiesis that continues for a period up to three weeks, and to develop a quantitative measure of erythrocyte production. HIM alone, free of hemopoietic stem cells, can be obtained by irradiating marrow biopsy material with 1000 rads, and suspensions of stem cells can be prepared from peripheral blood. *In vitro* hemopoiesis can be produced in the organ culture system by the addition of stem cells from one individual to the sterile microenvironment of another. Efforts are currently underway to refine the present system so that suspensions of stem cells can be quantitated; and methods are being sought to obtain increased numbers of stem cells from the peripheral blood.

MF12.524.013-1003AG6C

SCREENING FOR ERYTHROCYTE G6PD DEFICIENCY AND HEMOGLOBIN S. L.G. Dickson and A.E. McKee. NMRI, NNMC, Bethesda.

The goal has been the development and application of automated methods for screening military populations for erythrocyte glucose-6-phosphate dehydrogenase (G6PD) deficiency and hemoglobin S. G6PD

deficiency predisposes people to drug-induced hemolytic anemia. Apparently any oxidative drug will cause hemolysis. Antimalarial prophylactic and chemotherapeutic agents have caused serious hemolysis in small numbers of the military. Prior screening will allow preventing or minimizing the risk by adjustment of assignments or modification of therapeutic measures for malaria and other diseases. Persons with the homozygous hemoglobin S state are excluded from the stress of military service when detected. Those with the heterozygous hemoglobin S state, or the trait, are accepted for the performance of most duties. There now is evidence that the presence of the trait may be associated with morbidity and mortality. The exact nature and extent of this risk, or risks, remain to be determined.

Availability of economical screening methods for these two unrelated hereditary abnormalities will allow evaluation of the hazards they present and enhance selection of personnel for safe performance of duties. The method developed for G6PD screening is fluorometric, linear and zero order. This has been combined on a two-channel instrument with a modified dithionite method developed by the U.S. Army. Both methods have proven to be sensitive and precise for screening purposes. False positive results occur only with the presence of non-S sickling hemoglobins, a rare circumstance in the U.S. population. Progress has allowed initiation of screening programs for recruits and other populations.

MR041.20.01-0326A2GX

COAGULATION CHANGES AFTER TRAUMA AND SEPSIS. E.F. Hirsch; J.R. Fletcher; R.B. Moquin; R. Dostalek; S. Lucas and E. Perlin. Surgery Research Unit, NSA, DaNang, RVN; NMRI; and Naval Hospital, Bethesda.

A study of 18 American servicemen who had sustained battle injuries and developed sepsis were evaluated at the Division of Surgical Research, NSA, DaNang, RVN. In addition to treatment of injuries, clinical support and hemodynamic monitoring, the following coagulation parameters were serially determined: Clotting time, prothrombin time, activated partial thromboplastin time, platelet count, fibrinogen, fibrin split products (FSP) by immunoprecipitin technique, and serial thrombin time.

Statistically significant changes were observed for most of the coagulation parameters when they were compared with normal values, and when the values of survivors and nonsurvivors were compared. Fibrinogen levels were not significantly altered. The presence of FSP proved to be a poor prognostic sign. The presence

of FSP in association with hypotension and metabolic acidosis, despite an elevated cardiac output, was uniformly fatal. The classical syndrome of disseminated intravascular coagulation (DIC) was observed in only one instance as a near-terminal event in the presence of overwhelming sepsis.

Patients who are in shock, septic, or who have conditions that predispose to DIC, are now under study at the Naval Hospital, Bethesda. In addition to the above parameters, their coagulation is being studied with the use of newer techniques such as factor analysis, protamine gelation, staphylococcal clumping, and detailed analysis of the fibrinolytic system.

MR041.20.01-0041A2HE

THE EFFECTS OF CHEMICAL MODULATORS ON HEMOGLOBIN FUNCTION IN ITS RESPONSE TO TISSUE HYPOXIA. L.A. Kiesow; J.B. Shelton and J.W. Bless. Naval Medical Research Institute (NMRI), Bethesda.

The oxygen transport function of red blood cells adapts to hypoxic states of tissues which may result from trauma or septicemia. Chemical factors affecting this adaptation of red cell metabolism and red cell hemoglobin function are being investigated. A method for the rapid, continuous recording of oxygen dissociation curves, requiring only a few microliters of blood, has therefore been developed.

With this method, it became possible to study the direct effects of chemical compounds on the oxygen affinity of hemoglobin versus the indirect effects resulting from a metabolic response of the red cells. It could be shown thereby that creatine, one of the candidate molecules for red cell modifications, can permeate into red cells in the form of metal chelates. However, it does not directly affect the hemoglobin of red cells which had been stripped of organic phosphates intracellularly. On the other hand, 2,2-bis (hydroxymethyl)-2,2'-nitritotriethanol affects both the position of the oxygen dissociation curve relative to the oxygen partial pressure, and the shape of the curve, indicating direct and indirect modifications of hemoglobin.

M4305.05-0360A2GJ

FACTOR XIII INHIBITION IN PATIENTS ON ISO-NIAZID (INH) THERAPY. J.E. Kostinas and E.F. Cantow. Naval Hospital, Portsmouth, Va.

There have been several isolated cases of Factor XIII inhibition in patients receiving INH therapy for tuberculosis. The purpose of this study is to

determine if this inhibition is a significant finding in persons on INH therapy.

CICC 2-08-507

DEFIBRATION SYNDROME IN HYPOTENSIVE AND SEPTIC STATES RELATED TO COMBAT MEDICINE. J.E. Lang. Naval Hospital, San Diego.

In an attempt to better understand the syndromes of disseminated intravascular coagulation (DIC), 131 patients were studied intensively using a full battery of serial coagulation studies. Of these 131 patients, 88 had meningococcal disease, five had viral illnesses and 38 presented obstetrical problems. Laboratory data and clinical observations revealed that all patients in the gram-negative group demonstrated degrees of DIC which were classified as mild, moderate and severe.

The severe cases were recognized clinically by bleeding tendencies and probably represented the only form of DIC requiring therapy. Heparin therapy, in our study, alleviated the coagulation abnormalities providing hypotension and pH were corrected to normal ranges. Radial immunodiffusion studies for fibrinogen and fibrin split products revealed, unexpectedly, significant levels of fibrin split products in 98% of patients with meningococcal disease and in healthy, recruit blood donors. Factor V assay data indicated it to be a valuable laboratory procedure to detect mild or early DIC. The prothrombin time was prolonged greater than 3 sec in 78% of patients with meningococcal disease, whether or not the organism was recovered on initial spinal tap.

M4305.05-3033A2HX

USE OF NITROSOUREA COMPOUNDS IN MALIGNANT DISEASE. E. Perlin; R.F. Granatir; T.F. Ryan and R.B. Moquin. Naval Hospital, Bethesda.

The nitrosourea compounds are promising new chemotherapeutic agents which are currently undergoing clinical trials in patients with advanced malignant disease. We have treated thus far 15 patients with BCNU (bischloroethyl-nitrosourea) and five patients with 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU). The dose was generally 100 mg/m² BCNU given intravenously on two successive days, and 130 mg/m² CCNU per os. The drugs are given every 4-6 weeks.

The results in the BCNU group were as follows: Three out of six patients with Hodgkin's disease had a partial response (PR). One out of four patients with carcinoma of the stomach had a PR and is alive 2½ yrs after diagnosis (drug was given with 5-fluorouracil).

One out of two patients with glioblastoma multiforme had a PR. Two patients with melanoma, one with oat cell cancer of the lung and one with teratocarcinoma of the ovary failed to respond.

Of the CCNU group, one of two patients with adenocarcinoma of the lung had a PR (drug was given with hydroxyurea). One out of two patients with astrocytoma has stabilized following three months of drug therapy. One patient with carcinoma of the colon failed to respond.

Tolerable toxicity was observed and included nausea, vomiting, bone marrow depression 21-35 days after drug initiation, and mild vein irritation in patients receiving BCNU. The nitrosourea compounds appear to be helpful chemotherapeutic agents in patients with advanced malignant disease. These drugs seem to be particularly useful for Hodgkin's disease and malignancy of the central nervous system. When given early in the course of disease, they may be more effective.

CICC 2-06-304

TOTAL BODY POTASSIUM (K) AS A REFERENCE STANDARD FOR NORMALITY OF RED BLOOD CELL MASS. J. Sode; E.B. Scrom; B.L. Jernigan; W.M. Beckner and R.B. Moquin. Naval Hospital, Bethesda.

The red cell mass (RCM), when expressed in ml/kg of body weight, shows a wide standard deviation in the general population and single determinations of this parameter are clinically meaningful only when large variations from normal are recorded. In health, a major determinant of red cell production is the actively metabolizing lean body mass (LBM); excellent correlations between total body water (TBW) and RCM have been reported. Total body K (TBK), like TBW, is a constant function of LBM and can be determined conveniently in a whole body counter from the quantity of the naturally-occurring isotope ⁴⁰K in the body. For this reason, we measured TBK by whole body ⁴⁰K counting and RCM by ⁵¹Cr isotope dilution in 17 nonpolycythemic subjects whose body weights were 47.2 to 100.4 kg.

The correlation between RCM and TBK ($r = 0.94$) was superior to the one between RCM and body weight ($r = 0.73$), and 88% of the variance of RCM could be explained by the variance of TBK. Thus, TBK was a better reference standard for normality of RCM than body weight. A nomogram constructed from the experimental data permitted prediction of RCM in normal individuals with an acceptable degree of precision.

When TBK, instead of weight, is used as a reference standard for normality of RCM in a given individual, single determinations of RCM by ^{51}Cr isotope dilution can be made more meaningful in acute hemorrhage and other diseased states.
CICC 2-06-323

IMMUNOLOGY

ANTIBODY RESPONSE TO SPACED INTRADERMAL INJECTION OF AQUEOUS POLYVALENT INFLUENZA VACCINE. C.F. Bishop and J.L. Blair.
Naval Hospital, San Diego.

The antigenic response of Naval recruit personnel to influenza vaccine was studied employing subcutaneous or intradermal routes of injection. By subcutaneous injection 1 ml of vaccine was given, while 0.1 ml, spaced injections (2) were given intradermally. Formalinized saline was used for controls. Three blood samples were taken: one prior to injection, one at 14 days, and one at 28 days.

Comparable antibody titers for five viral antigens were obtained by hemagglutination inhibition micro-titer method showing twofold and fourfold antibody titer dilutions for the two routes of injection. Geometric mean titers were consistent in both types of injection. Local and systemic reactions to the vaccine reveal some disparity in percent of positive symptoms, the intradermal route causing less.
MR041.09.01-0113B9KL

SUPPRESSION OF DELAYED HYPERSENSITIVITY IN PATIENTS WITH ACUTE VIRAL HEPATITIS. L.A. Bucklew; P.R. Smith; M. Graf and J.B. Smith.
Naval Hospital, Bethesda.

Eighteen patients with acute viral hepatitis were tested for delayed hypersensitivity (DH) to seven common skin test antigens during acute hepatitis and after complete convalescence as measured by clinical and laboratory parameters.

On the basis of skin reactivity to these antigens, patients were divided into two groups. Twelve patients had complete anergy initially and six patients did not manifest initial anergy. Of the twelve anergic patients, nine had return of skin reactivity to normal and three remained anergic after complete convalescence. The six patients who were not anergic had little or no change in skin reactivity at the second testing. The frequency of rheumatoid factor, Australia antigen and

lymphadenopathy was higher in the anergic group than in the other group.

It may be that those patients with anergy have a higher incidence of immune-complex phenomena and are, perhaps, more likely to develop chronic hepatitis.
CICC 2-06-312

DETERMINATION OF GAMMA A IMMUNOGLOBULIN (IgA) DEFICIENCY IN BLOOD DONORS.

M.F. Dolan. Naval Hospital, Bethesda.

It is proposed to study the number of IgA deficient persons within the local Navy community and then to follow these patients for the development of autoimmune disease. There is evidence that IgA deficient persons are at high risk to develop autoimmune disease. A random screening of normal blood donors has set the incidence of IgA deficiency at one person in 500.

We draw about 9000 donors per year which should yield 18 persons with IgA deficiency. The ultimate goal is to identify an "at-risk" population who will be monitored for earliest possible therapeutic intervention. Autoimmune diseases are ordinarily diagnosed late and are associated with prolonged morbidity and high mortality. We have commenced the screening of donors.
CICC 2-06-310

THE SIGNIFICANCE OF AUSTRALIA ANTIGENEMIA IN APPARENTLY HEALTHY BLOOD DONORS. F.M. Griffin, Jr. Naval Hospital, Great Lakes.

The purpose of the study is to determine the significance of Australia antigenemia in apparently healthy blood donors. Six apparently healthy seaman recruits who were found to be hepatitis associated antigen (HAA) positive at the time of blood donation underwent an evaluation including history and physical examination, determination of liver function tests, and liver biopsy. Three had normal liver tissue on biopsy, two presented evidence of viral hepatitis, and one apparently suffered from chronic active hepatitis.

It appears that liver biopsy need be performed on this type of patient only if he has biochemical abnormalities of liver function in the absence of clinical illness characteristic of uncomplicated viral hepatitis.
CICC 2-13-007

DEFINITIVE IDENTIFICATION OF CIRCULATING LYMPHOCYTES. G.M. Penn; M.F. Dolan and R.F. Granatir. Naval Hospital, Bethesda.

Lymphocytes have previously been classified as B cells (bone marrow derived), or T cells (thymus derived), by utilizing fluorescein-tagged antisera to the immunoglobulins. B cells contain a significant quantity of immunoglobulin on their cytoplasmic membranes whereas T cells do not contain fluorescent-detectable immunoglobulin. With this methodology circulating lymphocytes from normals have been shown to have 15%-20% B cells. In addition, the quantity of fluorescent-detectable immunoglobulin on these B cells is not constant. In contrast, patients with chronic lymphatic leukemia have a significantly higher percentage of B cells, all of which have the same quantity of fluorescent-detectable immunoglobulin on their cytoplasmic membranes.

We are studying the circulating lymphocytes of patients with histologically-proven lymphomas, by the above methodology. We believe that many of these patients will have an increased number of B cells with a uniform quantity of immunoglobulin, which will be correlated with the type of lymphoma and prognosis. If the hypothesis is valid, this methodology may aid in the diagnosis of hidden lymphomas and may also serve to further define lymphomas by a functional classification.

CICC 2-06-311

DYNAMICS OF ALPHA-FETOPROTEIN (AFP) SYNTHESIS IN NONNEOPLASTIC HEPATIC DISORDERS. J.B. Smith. Naval Hospital, Bethesda.

AFP, a normal circulating human fetal alpha-1-globulin, disappears from the serum in the perinatal period and reappears in that of some adults with primary hepatoma and germinal testis/ovary cancers. AFP has been used diagnostically for these tumors.

Recently we used a sensitive double antibody counter-electrophoretic method (Sandwich CEP) to show that AFP can be detected transiently in small amounts (< 1.0 microgram/ml) in 2nd and 3rd trimester maternal serum and in acute viral hepatitis, particularly that associated with Australia antigen, Au (1). Clinical data were reviewed on seven patients with Au (1) viral hepatitis who had transient synthesis of AFP during their illness. Serum was studied at least weekly; AFP appeared in a mean of 12 days after liver function tests (LFT) reached peak values (range: 0-26 days). Mean peak serum glutamic oxalic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) values, before the appearance of AFP, were 1080 and 864

I.U. respectively; when AFP appeared, they were 225 and 150 I.U. Serial postoperative serum samples taken from a patient who had undergone partial hepatectomy after liver trauma revealed the presence of AFP (approx. 0.5 microgram/ml) on the 6th and 7th postoperative days. Histopathologic examination of the resected liver showed neither hepatitis nor hepatoma. LFT abnormalities were mild throughout the course, and the patient remained well after convalescence.

Retrodifferentiation of cells, with gene derepression occurring during hepatic reparative periods, is probably the basis for AFP synthesis.

CICC 2-06-312

OCCURRENCE OF ALPHA-FETOPROTEIN IN ACUTE VIRAL HEPATITIS. J.B. Smith. Naval Hospital, Bethesda.

Alpha-1 fetoprotein (AFP) is an alpha-1 globulin normally present in embryonic serum. Its occurrence in adult serum is usually felt to be consistent with the presence of germinal cell or primary hepatic neoplasms. Using a very sensitive double antibody counter-electrophoretic technique, AFP was demonstrated transiently in serum taken from six out of eleven patients during the course of viral hepatitis caused by Australia antigen, Au (1)/HAA, but not in any of eleven patients with viral hepatitis not associated with Au (1).

Clinical and laboratory comparison of the severity of hepatitis in the two groups was not significantly different, and it is postulated that synthesis of AFP during acute viral hepatitis may be related to gene derepression somehow related to infection with the Au virus.

CICC 2-06-312

LIVER-SPECIFIC ANTIGEN IN ADULT SERUM.

J.B. Smith and M. Iverson. (National Institutes for Medical Research, Mill Hill, London, England); Naval Hospital, Bethesda.

Three hundred eighty serum samples from 285 patients were studied by micro-double diffusion using rabbit anti-mouse liver antiserum for the occurrence of F antigen, a liver-specific intracellular gamma globulin isolated by Fravi and Lindenmann in 1968 (Nature 216:1968). This antigen, which is released into the serum during the course of hepatocellular destructive diseases, was found transiently in serum from eight of 25 patients with hepatic steatonecrosis. F antigen was also found in two of eleven patients with primary hepatoma and in four of eleven patients with secondary hepatic cancer. It was not found in

serum from patients without hepatic disease, normal persons, nor in patients on hemodialysis.

It is felt that the appearance of this antigen in serum indicates relatively severe hepatic damage and that detection of F antigen will prove to be a clinically useful test.

CICC 2-06-312

ALPHA-FETOPROTEIN (AFP) AND LIVER-SPECIFIC ANTIGEN IN SERUM DURING THE COURSE OF VIRAL HEPATITIS CAUSED BY HEPATITIS-ASSOCIATED ANTIGEN (HAA). J.B. Smith and L.F.

Barker. (Division of Biological Standards, NIH, Bethesda, Md.); Naval Hospital, Bethesda.

Serial weekly serum samples from 15 patients with hepatitis caused by HAA were studied for the occurrence of alpha-fetoprotein (AFP) and liver-specific (F) antigen. Eleven of 15 patients had detectable AFP at some time during the course of viral hepatitis and five of 15 patients had transient F antigen in the serum. In three cases, F antigen appeared just prior to AFP synthesis; in one case it appeared during the period of AFP production. In one case F antigen was not associated with AFP synthesis. In each icteric case, AFP appeared one to 8 weeks after peak HAA titers and 0-3 weeks after peak total bilirubin levels were reached.

Hepatocellular infection with HAA, destruction of hair cells with resultant release of F antigen into the serum, and gene derepression resulting in AFP synthesis during regenerative phases of hepatitis are felt to be important phenomena occurring during the course of viral hepatitis.

CICC 2-06-312

INFECTIOUS DISEASE

QUANTITATIVE NEWBORN GASTRIC CULTURES.

P.J. Goscienski and D. Schmottlach. Naval Hospital, San Diego.

There is no objective measure by which the risk of sepsis can be assessed in infants born to mothers with premature rupture of membranes. Although routine cultures of neonatal gastric contents have not been helpful, it is possible that quantitative culture of such material may be informative, as in the case of urinary tract infections.

Utilizing quantitative techniques which have been successfully applied to sputum culture, we are assessing the value of such methods in relation to routine

laboratory and clinical measurements. An attempt at objective assessment of clinical findings is represented by the "septiscore," by which point values are assigned to pertinent historical and observational data. No pathogens have been recovered from control infants to date, or from one suspect infant enrolled in the study.

Background studies of normal neonatal gastric juice indicate that coliform organisms survive, but do not multiply, in gastric juice under refrigeration. Parallel studies confirm that a large percentage of normal, newborn infants have neutrophils in smears of gastric contents, that bacteria may also be present on smear, but cultures are usually negative.

CICC 2-16-413

MENINGOCOCCAL POLYSACCHARIDE ANTIGEN AND HUMORAL ANTIBODY RESPONSE IN PATIENTS WITH MENINGOCOCCAL INFECTIONS.

T.A. Hoffman and E.A. Edwards. Naval Hospital, San Diego.

The significance of serum and cerebrospinal fluid (CSF) levels of meningococcal antigens (Ag) and the specific antibody (Ab) response was assessed in 87 patients with group C meningococcal disease. Levels of Ag were measured by counterimmunoelectrophoresis (CEP) and antibody was determined by bactericidal (B), hemagglutination (Ha), and complement fixation (CF) techniques.

Serum Ag were present in only one of 33 cases of acute meningococcemia, but in all 13 cases of fulminant meningococcemia and in eleven of 41 cases of meningitis. The level of Ag ranged from 0.02 to 1.25 micrograms/ml before therapy and correlated inversely with the pretreatment platelet count ($p = < 0.01$). Ag was detected by CEP in CSF in 65% of patients proven to have meningitis. High levels (5 to 20 micrograms/ml) were present in patients with meningoen- cephalopathy. These findings indicate that levels of Ag in pretreatment serum and CSF provide important prognostic data.

Changes in B and Ha Ab occurred concurrently and preceded the rise in CF Ab. Fourfold increase in B Ab occurred in: 65% of the meningococcemia patients within 24 hours, 73% of meningitis patients by 48 hours, and 70% of the serum antigen positive cases by 72 hours. These findings may indicate that the specific humoral response determined the form of clinical disease which occurred.

MR041.20.01-0385A2GI

MICROBIOLOGICAL SURVEILLANCE OF LEUKEMIA PATIENTS. H.M. Koenig; J.A. Campbell and P.J. Goscienski. Naval Hospital, San Diego.

Bacterial and fungal infections are responsible for much of the morbidity and early mortality in children with acute leukemia. Infections in these children often arise from resident flora during periods of lowered host resistance due to the primary disease process and the therapy directed against this process. Frequent microbial monitoring of selected sites can identify changes in resident flora or increasing numbers of particular organisms which might become pathogens.

All children undergoing treatment for acute leukemia at this facility submit blood, throat, urine and stool cultures at their regular clinic visits. If sepsis is suspected, daily cerebrospinal fluid (CSF) cultures are also obtained. Basic bacterial and fungal culture techniques along with selective and special media are used to facilitate identification of organisms.

Nine children have now been cultured regularly for four weeks. During this period three children have suffered relapse of their leukemia, developed high fevers and appeared septic. One child has presented proven gram-negative septicemia due to an organism previously isolated from his throat. Positive blood cultures were not obtained for the other two children, but *Staph. aureus* was isolated from their throats. Lysis of their fevers occurred with the institution of anti-staphylococcal antibiotics.

CICC 2-16-415

THE NITROBLUE TETRAZOLIUM TEST. P.J. Kovalcik. Naval Hospital, Boston.

The nitroblue tetrazolium (NBT) test is being performed to aid in the diagnosis of postoperative fever. This test is based on the increased spontaneous reduction of pale yellow NBT dye to blue-black crystals by peripheral blood neutrophils in the presence of bacterial infection.

Since 3 Jan 1972, three patients undergoing major upper abdominal surgery at the Naval Hospital, Boston have been studied both preoperatively and for several days postoperatively. A flow sheet for correlating this test with more conventional parameters of surgical postoperative evaluation has been formulated. Although there are not yet sufficient numbers of patients for valid statistical conclusions, this test is feasible and offers promise in the evaluation of postoperative fever. CICC 2-02-107

A STUDY OF FOUR STRAINS OF SMALLPOX VACCINE: COMPARISON OF ADMINISTRATION ROUTE AND DOSAGE WITH MORBIDITY AND SEROLOGIC CONVERSION. J.E. Schanberger; P.J. Goscienski and J.D. Connor. Naval Hospital, San Diego.

Nine hundred children ages one through five years, with parental consent, will receive smallpox vaccination by a two-step procedure. The four vaccines are provided by the Infectious Disease Branch, National Institute of Allergy and Infectious Disease, National Institutes of Health.

Since Nov 1970, 355 children received their initial vaccination: 193 percutaneously, and 162 subcutaneously. No complications occurred in the percutaneous group. In the subcutaneous group no complications occurred with two of the vaccines. Temporary, local swelling and erythema occurred in five of the 24 recipients with the third subcutaneous vaccine and elevated temperature was observed in three of the five. The fourth subcutaneous vaccine injection was associated with temporary, local redness in two patients. The six-month follow-up in 17 patients from the subcutaneous group is in progress.

M4305.05-3058AGG2

NEOPLASTIC DISEASE

GALLIUM⁶⁷ SCANS IN THE STAGING OF CARCINOMA OF THE BREAST. E.M. Braun; T.J. Lapine and D.G. Taylor. Naval Hospital, Boston.

The concentration of the exogenously administered radioisotope gallium⁶⁷ is increased in malignant tissue as compared to normal tissue. In this study, whole-body scans are performed with a Gamma camera 72 hours after isotope administration to patients with suspected or proven breast cancer. The results of the pathologic examination of the surgical specimens are then correlated with the results of the scan. Areas of increased isotopic concentration outside the breast are also being investigated in hopes of identifying sites of metastatic disease. Selected tumors other than breast have also been studied.

Thus far, increased concentration of gallium⁶⁷ in benign breast disease has not occurred. In cases of breast and lung cancer, on the other hand, not only has known disease been delineated on the scan, but otherwise unrecognized sites of metastasis have also been identified. Areas involved with Hodgkin's

disease, including lymph nodes and liver, have also provided positive scans.

Careful long-term patient follow-up is planned in order to evaluate the true clinical usefulness of the gallium⁶⁷ scan.

CICC 2-02-111

NAVY COOPERATIVE CHEMOTHERAPY GROUP.

R.A. Burningham; J.E. Kostinas; G. Lang; R. Moquin and H. Shute. Naval Hospital, Philadelphia.

The many contributions of the various cooperative groups for the treatment of patients with malignant disorders has been well documented in the medical literature. Considering the large patient population, the qualifications and experience of many Navy medical officers, the opportunity to contribute to medical knowledge in this field, and in order to enhance our training programs, a Navy Cooperative Oncology Group was established. Currently the necessary forms are being processed for formal submission to the National Cancer Institute.

A protocol for the treatment of refractive or advanced acute myeloblastic leukemia using combination drug therapy — hydroxyurea, mercaptopurine, and dexamethasone — is being considered by the group. Protocols for use in disease oriented phase II studies using drugs such as methyl-CCNU (chloroethyl-cyclohexyl-nitrosourea), TIC mustard = 5-(3,3-BIS [2-chloroethyl]-1-triazeno)-imidazole-4-carboxamide, and guanzole are being formulated by various members of the Group. If feasible, it is anticipated that the studies can be expanded to involve all forms of malignancy with participation of all Navy medical facilities treating patients with malignant disorders.

CICC 2-05-609

CHEMOTHERAPY OF SELECTED BLOOD DISEASES (COLLABORATIVE STUDY).

R.A. Burningham; A. Suvani and J.E. Engeler, Jr. Naval Hospital, Philadelphia.

The Hematology/Oncology Branch, Medical Service has been a member of the Acute Leukemia Group B (ALGB) cooperative chemotherapy group since 1967. In 1970 the study was expanded to include nonhematologic malignancies when the Branch became a member of the Eastern Cooperative Oncology Group (ECOG). The essential goal of these groups is to systematically plan, initiate, execute, evaluate, analyze, and report on research methods of management and treatment of patients with neoplastic disease.

Ninety-seven patients have been randomized, by this hospital, into ALGB protocols as follows: multiple myeloma-3, Hodgkin's disease-stage III & IV-18, other malignant lymphomas-17, acute myeloblastic leukemias-19, acute lymphoblastic leukemias-10, chronic myelocytic leukemias-5, and various forms of solid tumors-25. In regard to ECOG protocols, 23 patients were entered into study as follows: carcinoma of lung-9, malignant melanoma-4, adenocarcinomas-5, and miscellaneous tumors-5.

Present emphasis and future direction of these groups is to: (1) improve duration of complete remission and possible cure of patients with acute lymphoblastic leukemia, (2) improve remission induction rates of patients with acute myeloblastic leukemia, (3) prevent or significantly delay the onset of blastic crisis in chronic myelocytic leukemia, (4) provide broader application of the principles of immunotherapy in neoplasia, and (5) expand the screening of drugs for antineoplastic activity in phase II disease-oriented studies.

MR041.20.01-0108A2GX

E.S.R. MEASUREMENTS ON HUMAN TISSUES AS A CANCER INDICATOR.

E.D. Finch and D.K. Heffner. Naval Hospital and Naval Medical Research Institute, Bethesda.

The purpose of this study is to explore the possibilities of using electron spin resonance (e.s.r.) spectroscopy measurements on human biopsy specimens to differentiate benign from malignant disease, and to use measurements on blood samples as a detector of cancer. Free radicals are quenched by freezing tissue samples to liquid nitrogen temperature. Studies to date on breast carcinoma indicate a two- to fivefold increase in the spin concentration in malignant tissue. No qualitative changes have been found in the e.s.r. signal.

These preliminary results, together with experimental animal studies done by others showing the appearance of free radicals in blood throughout the course of experimental cancer, offer encouragement for the further investigation of e.s.r. as a diagnostic aid.

CICC 2-06-308

THE SIGNIFICANCE OF POSITIVE IPSILATERAL NODES IN RESECTIONS OF LUNG.

R.G. Fosburg and M.J. O'Sullivan, Jr. Naval Hospital, San Diego.

Sixteen patients with primary carcinoma of the lung, found to have ipsilateral mediastinal lymph node involvement by mediastinoscopy, have been considered for thoracotomy after extensive anatomic and physiologic evaluation.

Seven patients have undergone radical pneumonectomy but there are only two survivors, 10 and 13 months postoperatively. Of seven patients explored and found unresectable, four have died and two now have distant metastases. One patient, considered a poor operative risk, was not explored; one patient developed a cervical metastasis before thoracotomy. Current results suggest a very ominous prognosis for positive ipsilateral nodes.

CICC 2-16-407

USE OF NITROSOUREA COMPOUNDS IN MALIGNANT DISEASE. E. Perlin; R.F. Granatir; T.F. Ryan and R.B. Moquin. Naval Hospital, Bethesda.

The nitrosourea compounds are promising new chemotherapeutic agents which are currently undergoing clinical trials in patients with advanced malignant disease. We have treated thus far 15 patients with BCNU-1, 3-bis(2-chloroethyl)-1 nitrosourea, and five patients with CCNU, 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea. The dose was generally intravenous 100 mg/m² on two successive days for BCNU, and 130 mg/m² per os for CCNU. The drugs are given every four-six weeks.

The results in the BCNU group were as follows: Three out of six patients with Hodgkin's disease had a partial response (PR). One out of four patients with carcinoma of the stomach had a PR and is alive 2½ years after diagnosis (drug was given with 5-fluorouracil), and one of two patients with glioblastoma multiforme had a PR. Two patients with melanoma, one with oat cell cancer of the lung and one with teratocarcinoma of the ovary failed to respond. Of the CCNU group, one out of two patients with adenocarcinoma of the lung had a PR (drug was given with hydroxyurea); one out of two patients with astrocytoma has had stability three months after drug initiation; and one patient with carcinoma of the colon failed to respond. Toxicity was tolerable and included nausea, vomiting, bone marrow depression 21-35 days after drug initiation, and mild vein irritation in patients receiving BCNU.

The nitrosourea compounds appear to be helpful chemotherapeutic agents in patients with advanced malignant disease, and seem to be particularly useful for Hodgkin's disease and malignancy of the central nervous system. When given early in the course of disease, they may be more effective.

CICC 2-06-304

SEARCH FOR SERUM DNA IN MALIGNANCY.

E. Perlin and R.B. Moquin. Naval Hospital, Bethesda.

In 1948 Niazi and State reported that when diphenylamine was added to the serum of patients with malignant tumors, an intense color reaction developed. The serum of patients with other diseases seemed to react similarly, however, and led Ayala, et al., to propose that the substance reactive with the reagent was the deoxyhexose content of sialic acid. The reaction is also useful for estimation of deoxyribonucleic acid (DNA) since diphenylamine also reacts with deoxyribose. In 1946 Tan, et al., found elevated DNA levels in three of 29 patients with lymphoid neoplasms using an immunoprecipitin technique.

Stimulated by this report, we tested the serum of 43 patients with malignant tumors using diphenylamine by the technique of Burton, with a modification by Croft and Lubran to obviate interference of sialic acid. The group included the following patients: cancer of the breast (8), Hodgkin's disease (7), lymphosarcoma (4), malignant melanoma (4), acute leukemia (8), chronic lymphatic leukemia (3), chronic myelocytic leukemia (1), and miscellaneous tumors (8).

Results indicate that 41 patients and 31 controls had no detectable DNA. In two patients with acute lymphatic leukemia (ALL), DNA levels were 25.5 mcg/ml and 4.5 mcg/ml respectively. Both patients had lymphoblast counts > 100,000/mm³. It is possible that the rapid release of large amounts of DNA into the circulation can be important clinically because DNA thromboembolism has been reported in acute leukemia after total body irradiation. Total body irradiation of normal rats, or rats bearing the Walker carcinosarcoma, does not appear to release detectable amounts of DNA into the serum, in experiments thus far.

MR041.20.01-0173A2HX

CHEMOTHERAPEUTIC AGENTS IN THE TREATMENT OF LUNG TUMORS. M.J. O'Sullivan, Jr. and R.G. Fosburg. Naval Hospital, San Diego.

The average survival of patients with diagnosed unresectable carcinoma of the lung is eight months. This figure is valid despite the use of radiotherapy or previously available chemotherapeutic agents. New and promising agents have, however, become available in the recent past.

In association with the National Cancer Institute, CCNU, a nitrosourea compound, is being evaluated.

Statistically significant data is not yet available to determine its efficacy in the enhancement of the quality or duration of survival.
CICC 2-16-405

TESTICULAR TUMORS: A STUDY OF MULLERIAN-INHIBITING SUBSTANCE. P.C. Walsh; J.M. Christianson and M.B. Rotner. Naval Hospital, San Diego.

Testicular tumors are one of the most common forms of malignancy in men aged 20 to 35 years. Because these tumors are frequently diagnosed after metastatic spread has occurred, a method for their earlier detection is needed.

Experimentally, the transplantation of fetal genital ridge tissue into the adult testis produces teratocarcinoma. During fetal life, the testis produces a nondialyzable, nonsteroidal substance which causes regression of Müller's ducts. This substance, Mullerian-inhibiting substance (MIS), is not produced by the adult testis. Because testicular tumors are known to produce other hormones and because these tumors may arise from embryonic elements, their ability to produce MIS is being tested.

Explants of testicular tumors are incubated with 14-day-old fetal rat Mullerian ducts in organ culture. The production of MIS is documented by histological regression of the Mullerian ducts after three days of incubation. If the presence of MIS in testicular tumors is documented, it will be important to search for urinary excretion of MIS in patients with these tumors.
CICC 2-16-403

PROSPECTIVE STUDY OF HEPATIC SCAN IN DETECTING METASTASES IN SERVICEMEN. G.J. Weir, Jr. and R.E. Pries. Naval Hospital, Great Lakes.

Surgical exploration of the abdomen, liver function studies and hepatic scintigraphy have all been used to detect malignancy metastatic to the liver. This study is designed to determine what percentage of hepatic metastases are detected by each procedure and how many false positive diagnoses are made.

Scintigraphy and liver function studies will be performed on 100 consecutive patients who have malignancy and are undergoing abdominal exploration. Scintigraphy, liver function studies and clinical evaluation will be performed at six and twelve months after surgery to detect metastases which were missed.

Fifty-one patients have been entered in the study to date and 23 have been followed for twelve months or until death. Fifteen of these 23 were free of hepatic

metastatic disease; eight were not. In the 23 patients with normal livers, one had a positive and one an equivocal scan. Three had abnormal alkaline phosphatase, one had abnormal bilirubin and one abnormal BSP retention. Of the eight with hepatic metastases, three were detected by scan, three at surgery; three had elevation of alkaline phosphatase, one had elevation of bilirubin and one elevation of BSP retention. At this point the hepatic scan and surgical exploration are equally accurate in detecting metastatic hepatic disease; both are more accurate than liver function studies. There was one false positive and one equivocal scan. Three patients with abnormal liver function studies (one had abnormalities in all three tests, two in the alkaline phosphatase only) had no evidence of metastatic disease. There were no false positive results from surgery.
MR041.20.01-0367A2GJ

NEUROLOGY

CORRELATION OF NEONATAL EEG WITH GESTATIONAL AGE AND DISEASE STATES. D.W. Bailey and S.G. Larson. Naval Hospital, Bethesda.

Clarification of the potential role of the electroencephalogram (EEG) in the management of newborns with potential problems or proven disease is needed. Estimation of gestational age, evaluation of the effects of hypoxia or sepsis on the central nervous system, and determination of etiology and prognosis in neonatal seizure disorders can be enhanced when serial EEGs are added to other established clinical and laboratory procedures.

EEG studies on all neonates admitted to the Intensive Care Nursery, with selected controls, are planned with neurologic and EEG follow-up for a minimum of two years.

CICC 2-06-326

EVALUATION OF PERIPHERAL NERVE REPLACEMENT BY LYOPHILIZED ALLOGRAFT FOR THE TREATMENT OF COMBAT-INDUCED INJURY.

J.W. Hammon, Jr.; H. Boffman and G.W. Cady. Naval Hospital, San Diego.

This study is designed to evaluate the feasibility of using collagen-wrapped lyophilized allografts for the treatment of combat-induced injury. A series of animals will have sciatic nerve segments replaced by allografts and evaluated by a nerve function monitoring

system under design and construction by Geoscience Ltd., Solana Beach, Calif., under Office of Naval Research (ONR) contract. A series of rabbits have been so grafted and are under study using the above techniques.

M4305.05-3067AG52

PERCUTANEOUS CERVICAL CORDOTOMY. J.B. Oldershaw and C. Ochs. Naval Hospital, Great Lakes.

Cordotomy is a proven method of controlling pain in patients with malignancy. Operative cordotomy is hazardous in many patients with malignancy. Percutaneous cordotomy has been developed as a safer means of providing these patients with pain relief.

The technique of percutaneous cordotomy has been developed utilizing Dr. Sean Mullan, University of Chicago, as a consultant. Equipment for the procedure has been ordered; no patients have been studied as yet. CICC 2-13-020

CEREBRAL AND SUPRASEGMENTAL DETERMINANTS OF MUSCLE CELL DIFFERENTIATION.

H. Travers. Naval Hospital, Portsmouth, Va.

Recent research into skeletal muscle development has led to the concept of motor unit uniformity where muscle cells differentiate biochemically and morphologically in a manner specific to the type of motor neuron which innervates them. Those factors important in the differentiation of type-specific lower motor neurons have yet to be completely elucidated. There is some evidence that suprasegmental structures may influence the maturation of the motor unit.

In order to clarify the developmental effects of upper motor neurons on lower motor neurons and, ultimately, muscle cells early in embryonic life, Wistar rat fetuses were subjected to intra-uterine decapitation on the 16th day of gestation. At-term fetuses were taken by cesarean section; the normal and decapitated animals were sacrificed and the hind legs were sectioned at comparable levels and stained histochemically for adenosine triphosphatase, phosphorylase, and succinic dehydrogenase — techniques which separate muscle cells into two distinct types of muscle fibers. Preliminary comparison of tissue taken from normal and decapitated fetuses indicates a possible role for the upper motor neuron in motor unit cytodifferentiation.

CICC 2-08-515

NEUROSURGERY

EVALUATION OF PROGRESS OF HEAD INJURY PATIENTS FROM VIETNAM. F.E. Jackson. Naval Hospital, Camp Pendleton.

Thirty-two consecutive patients from Vietnam with head injuries due to missile wounds have been studied and subjected to detailed clinical, radiologic and clinical psychological testing on the Neurosurgery Service. These patients have now been followed an average of 2½ years; their resultant symptomatology has been correlated with location, depth, multiplicity of wounds, and side of hemispherical dominance.

Eight (8) manuscripts have been published concerning the initial treatment and progress of this group of patients.

M4305.05-0002AGG2

VASCULAR COMPLICATIONS OF HEAD INJURIES AND MISSILE WOUNDS OF THE BRAIN RESULTING FROM THE VIETNAMESE CONFLICT. F.E. Jackson. Naval Hospital, Camp Pendleton.

In addition to the more usual types of vascular complications of missile wounds, advanced techniques in neuroradiology have enabled military surgeons to identify by angiographic procedures hitherto poorly understood and documented complications of missile and blunt injuries to the brain. Typical examples are: delayed arterial and arteriovenous aneurysm formation; delayed "spate" thrombosis of cerebral arteries, veins, and sinuses; and delayed subdural hematoma formations.

On the neurosurgery service at the Naval Hospital, Camp Pendleton, a large number of wounded service members with brain wounds sustained in Vietnam have been studied by these techniques. Following appropriate treatment, their cases have been documented and published. Seven (7) manuscripts have been published in 1971 on this subject alone, with the help of this grant. Additionally, a new type silicone-rubber flexible suction catheter with a sterile reservoir, non-collapsible walls and radiopaque side markings, has been developed.

This "brain drain" is now being increasingly utilized by civilian and military neurosurgeons for drainage of subdural hematomas, replacing previously-used Penrose drains and avoiding the wet and soiled head dressings that were commonplace following Penrose drainage of subdural hematomas. This drain has been named the "Jackson-Pratt" drain.

M4305.05-0003AGG2

EVALUATION OF PNEUMATIC CRANIOTOMES FOR BRAIN SURGERY IN VIETNAM CASUALTIES.

F.E. Jackson. Naval Hospital, Camp Pendleton.

Pneumatic craniotomes have provided a fast and relatively bloodless method of performing a craniotomy both in Vietnam and in CONUS. Representing a relatively new advance, they have now been widely accepted and used by military and civilian neurosurgeons. Provisions for installation of high pressure air and nitrogen systems to actuate pneumatic tools are now being made in the operating rooms installed in new hospitals, not only for neurosurgery, but also for use in orthopedic, oral and ENT surgery. Refinements in the instrumentation and technique of using these pneumatic instruments has been aided by this grant; twelve clinical papers, two booklets (Clinical Symposia) and one teaching movie have resulted from the author's work in the initial development of these surgical instruments.

Current research deals with the clinical and radiologic evidence of bone healing following the use of pneumatic surgical instruments. This year, biological and engineering studies concerned with temperature, pressure, developed torque and histological and physiological response of osteoblasts along the incised edge of bone have been initiated. The principal investigator has been appointed as a member of the Instrument Committee of the Harvey Cushing Society (American Association of Neurological Surgeons), with whom this research is being coordinated.

M4305.05-0002AGG2

INTRACRANIAL VASOSPASM. **B.L. Rish.** Naval Hospital, Bethesda.

This project is designed to investigate the tolerance and efficacy of vasospasmolytic agents in experimental subarachnoid hemorrhage. A microsurgical exposure of the basilar artery in dogs is used to photographically and fluoroscopically document subarachnoid hemorrhage-induced vasospasm and the alterations secondary to intracarotid vasospasmolytic agents. The laboratory is being relocated at the Armed Forces Radiobiology Research Institute (AFRRI), Bethesda. Completion of protocol and report is planned for next year.

MR041.20.01-0332A2GX

MICROSURGICAL INTRACRANIAL VASCULAR REPAIR AND AUTOGENOUS SHUNTING TECHNIQUES. **B.L. Rish.** Naval Hospital, Bethesda.

The microsurgical use of autogenous vein material is being explored for vascular repair and development of a cerebrospinal fluid shunt in the hydrocephalic state.

The microsurgery research laboratory is being relocated at the Armed Forces Radiobiology Research Institute, Bethesda, and work in microvascular technique will be continued at that facility.

MR041.20.01-0333A2GX

OBSTETRICS-GYNECOLOGY

EVALUATION OF A RAPID PREGNANCY TEST ON 1000 PATIENTS. **R.L. Baker and J.C. Shaffer.** Naval Hospital, Portsmouth, Va.

A new pregnancy test using dry, impregnated disposable paper slides* is being evaluated. These reagents do not require refrigeration and offer simplicity of performance, using one drop of tap water and one drop of the patient's urine. The test results will be correlated with other rapid pregnancy tests and patient outcome to determine accuracy, sensitivity, and reliability. The first 50 tests have yielded accurate correlation, both positive and negative.

CICC 2-08-509

CHEST X-RAY STUDY OF 1000 POSTPARTUM PATIENTS TO DETERMINE THE INCIDENCE OF PNEUMOPERICARDIUM AND PNEUMOMEDIASTINUM. **R.L. Baker and J.A. Sebastian.** Naval Hospital, Portsmouth, Va.

Posteroanterior and lateral chest X-rays are to be performed on 1,000 newly delivered patients. The length of labor and the second stage, complications, and postpartum morbidity, will be correlated with the chest findings. The senior author has a small series of case reports of these rarely-reported entities and suspects that these findings may be relatively common if searched for.

CICC 2-08-517

SERUM HEXOSAMINIDASE B LEVELS IN PATIENTS WITH EXCESS WEIGHT GAIN IN PREGNANCY.

R.C. Cefalo; R.S. Juskevich and J.J. McCartney. Naval Hospital, Bethesda.

Excess weight gain in pregnancy is associated with a high incidence of toxemia. Serum hexosaminidase B levels have been reported to be markedly elevated in patients with excess weight gain and edema of

*Dri-Dot™, Organon, Inc.

pregnancy. This elevation may be due to a dysfunction that may manifest itself early in pregnancy.

Serum hexosaminidase B levels and liver dysfunction tests will be performed in patients with excess weight gain, with matching "normal" controls in each trimester, and in patients with antepartum and/or intrapartum toxemia of pregnancy.
CICC 2-06-347

INTRAVENOUS AND ORAL GLUCOSE TOLERANCE TESTS IN PREGNANCY AS RELATED TO PERINATAL MORTALITY AND/OR CONGENITAL ANOMALIES. J.J. O'Neill and R.C. Drips. Naval Hospital, Great Lakes.

Oral and intravenous glucose tolerance tests were performed during the third trimester of pregnancy in 50 patients considered at high risk for diabetes mellitus.

The oral test was found to be abnormal in 69% of the patients tested. The intravenous test was abnormal in 39%. Congenital anomalies were more frequent in the patients with the abnormal intravenous test. Thus, the intravenous test was more selective since only about one-half the number of patients tested were abnormal; at the same time, it was more sensitive to complications since it identified two more patients with complications than did the oral test.
MR041.20.01.0323A2GX

TREATMENT OF DYSPLASIA AND IN-SITU CARCINOMA OF THE CERVIX WITH CRYOSURGERY. R.T. Upton and R.L. Baker. Naval Hospital, Portsmouth, Va.

Early, noninvasive neoplasia of the uterine cervix may be efficaciously managed in selected cases by means of cryosurgery.

In an ongoing study started in Jan 1969, 128 patients with mild, moderate, or marked dysplasia or in-situ carcinoma of the uterine cervix were thoroughly evaluated with colposcopy, endocervical curettage and direct cervical biopsy. This group of patients with negative endocervical curettage was treated with cryosurgery. Cure rates vary from 66% with a small group of patients with in-situ carcinoma to 89% of those with mild dysplasia.

Cryosurgery in carefully-selected patients with early noninvasive cervical neoplasia, who wish to maintain childbearing capability, offers an effective alternative to the previous standard cold-knife conization method of management.
CICC 2-08-501

OPHTHALMOLOGY

A CLINICAL STUDY OF A DISTINCT TYPE OF EYE DISEASE, "FOVEOMACULAR RETINITIS," IN MILITARY PERSONNEL. B.R. Blais; R.L. Marlor; D.G. Boyden and F.R. Preston. Naval Hospital, San Diego.

This is a distinct type of eye disease involving primarily the fovea. It occurs predominantly in young, enlisted, military personnel usually involving both eyes and resulting in primarily impaired central vision. The study entails a retrospective study: Phase I: Incidence of disease at the Naval Hospitals San Diego, Camp Pendleton, Great Lakes, and Beaufort, during the years 1965-1969. Phase II: Descriptive study of cases at Naval Hospitals San Diego and Camp Pendleton, in 1968-1969. Phase III: Case control study of new cases admitted to Naval Hospital, San Diego.

During the period 1965-1969, 308 cases were found in the four institutions noted. The majority of the cases had experienced onset in the San Diego area. Marine recruits were at the highest risk of developing the disease. Detailed epidemiological study of the cases failed to reveal any common factors of etiological significance.

M4305.05-3064AGG2

VISUAL ELECTROPHYSIOLOGICAL RECORDING SYSTEM. B.R. Blais; C.T. White and D.G. Boyden. Naval Hospital, San Diego and Naval Electronics Laboratory Center, San Diego.

A simplified system for obtaining records of certain electrophysiological events which are produced by visual stimulation, especially the visual-evoked cortical potential (VECP) and the electroretinogram (ERG), is being developed. It will be employed for study of certain macular diseases and other conditions affecting visual efficiency.

M4305.05-3077AGG2

EFFECTS OF NORMAL LABOR AND DELIVERY ON INTRAOCULAR PRESSURE IN HUMANS. D.G. Boyden; J.B. Lench and T.O. Paul. Naval Hospital, San Diego.

The purpose of this investigation is to determine the effects of normal labor and delivery on intraocular pressure in humans, in order to clarify the indication for cesarean section on termination of pregnancy in patients with marginal corneal dystrophy, recent ocular trauma, or ocular surgery.

Base line ocular examination, including applanation tonometry, will be performed in pregnant humans. During subsequent labor and delivery, measurements and intraocular pressure during uterine contraction and relaxation will be made.

CICC 2-16-401

THERMAL CYCLODIALYSIS: A NEW SURGICAL TECHNIQUE FOR THE TREATMENT OF GLAUCOMA. D.L. Brooks; W.R. Wilson and H.T. Friebe. Naval Hospital, Philadelphia.

Most antiglaucomatose operations owe their effectiveness to an improvement of the outflow of fluid from the eye. These filtering operations, as they are called, drain fluid from the intraocular spaces to extraocular spaces. The cyclodialysis, however, drains fluid from one intraocular space to another and is employed in this country mostly in aphakic patients. This operation has certain advantages over the filtering operations. For this reason, the present study is undertaken to develop certain modifications of the cyclodialysis operation in order to make it useful in the phakic patient.

Several proposed modifications will be tested in a series of animal experiments for the duration of this study. The most successful modification can then be used in a large animal series and, if indicated, in difficult human glaucoma cases.

CICC 2-05-611

ORTHOPEDICS

THE TREATMENT OF REFRACTORY OSTEOMYELITIS WITH HYPERBARIC OXYGEN. E.L. Bingham; G.B. Hart; R.E. Thompson and E.E. Mainous. Naval Hospital, Long Beach.

This is a preliminary study to ascertain the possible effectiveness of hyperbaric oxygen (OHP) in effecting a remission in refractory osteomyelitis.

Forty-three patients were treated with OHP at two atmospheres absolute, two hours per day until remission was effected, or for a sum total of 40 compressions. The osteomyelitis was regionally classified as follows: Extremity (23), spine-pelvis (four), chest wall (five), skull and facial (eleven). All patients improved with OHP as noted subjectively by decreased bone pain and objectively by decreased drainage, or closure of fistula with later breakdown. Thirty-one patients proceeded to complete healing, by closure of fistula and resolution of bone abnormalities with no breakdown;

20 patients have been followed for two years or more. Osteomyelitis of the skull and facial bones responded more favorably (92%) and the spine-pelvis category gave the poorest (50%) response. The most frequent organisms cultured were: *Staphylococcus aureus*, coagulase positive; *E. coli*, and; *Pseudomonas aeruginosa*.

Refractory osteomyelitis responds favorably to OHP, effecting a remission in 72% of cases thus treated. A double blind randomized study with crossover is in progress.

M4306.01-3034AGG2

TWO-STAGE TENDON GRAFTING. J.C. Brothers and J.G. deWaal. Naval Hospital, Boston.

The use of silastic material has been shown to produce a smooth nonadhering surface when inserted in the human body. The use of a silastic rod prior to tendon grafting should produce a tunnel whose lining has little or no tendency to produce adhesions, permitting free gliding of an inserted tendon graft.

At the Nav Hosp, Boston, severely injured hands requiring tendon grafts to restore active finger flexion have been treated by a two-stage technique of inserting the silastic rod for six to eight weeks prior to the tendon graft. Passive motion is encouraged while the rod is in place; the rod is attached to the distal phalanx but is left free in the distal forearm. The tendon graft is placed in the newly-formed tunnel and the tendon-to-tendon juncture is allowed to rest in the tunnel also. Postoperative management allows early gentle passive motion with unrestricted motion at six weeks. Five tendon grafts have been inserted using this method with two excellent, two good, one fair and no poor results, according to the Boyes' method of rating finger function after tendon grafting.

Fingers with severe tendon injuries requiring tendon grafts can be treated very satisfactorily by a two-stage technique, utilizing a silastic rod as the first stage to form a nonadhering bed in which the tendon graft can function.

CICC 2-02-112

CAST-BRACE TREATMENT OF FEMORAL SHAFT FRACTURES. J.C. Brothers and J.G. deWaal. Naval Hospital, Boston.

A properly applied cast-brace allows femoral fracture healing while also permitting ambulation and functional motion of the hip and knee joint of the involved extremity. At Nav Hosp, Boston nine patients with

femoral shaft fractures have been treated by this method after an initial three to eight weeks of skeletal traction.

Six have healed and now are fully ambulatory without support; five of these six healed within six months. Two others are still under treatment and there has been one failure. Knee flexion in the cast brace measures 60 to 90 degrees from neutral in most patients; all patients have 70 to 80 degrees of hip flexion from neutral. Further motion improves rapidly after removal of the cast-brace. While in the cast-brace, all patients become ambulatory with support and 50% require no support after four weeks. The one failure required an intramedullary nailing; it was a proximal fracture.

Use of the cast-brace is a new and practical method of managing femoral shaft fractures by an ambulatory nonoperative technique after an initial few weeks in skeletal traction. Proximal fractures should be carefully selected and closely followed.

CICC 2-02-113

TREATMENT OF TIBIAL FRACTURES WITH ELECTRIC MICROCURRENT. **G.W. Cady; J.M. Casey and C.T. Brighton.** Naval Hospital, San Diego.

Hospitalized patients with stress fractures of the upper tibia who meet a set of defined criteria will have a direct electric current (about ten microamperes) administered to the affected leg through a K-wire cathode inserted into the fracture site under local anesthesia. The anode of the small battery pack will be taped to the skin and a nonweight-bearing cast will be applied. Physical and X-ray examinations will be repeated periodically until clinical evidence of complete healing has been achieved. The investigation is being conducted as a control, double blind, clinical, pilot study.

The first patients are being treated with this therapy and none have completed the course at this time.

M4305.05-3079AGG2

COMPARISON OF PARTIAL AND TOTAL RESECTION OF THE MEDIAL MENISCUS IN THE DOG'S KNEE. **J.S. Cox.** Naval Hospital, Oakland.

The results of total meniscectomy in military active duty personnel have frequently been less than satisfactory, resulting in prolonged convalescence. In an effort to correct this problem a study has commenced to compare results of removal of the entire medial meniscus and removal of only the medial rim of the meniscus.

To date, ten of the twelve dogs scheduled have been operated on and observed. Initial results suggest that leaving part of the dog's meniscus lessens the

subsequent appearance of degenerative changes. It should be kept in mind these results are incomplete, therefore inconclusive.

MR041.20.01-0337A2GX

STIMULATION OF FRACTURE HEALING BY EARLY FITTING OF WEIGHT-BEARING BRACES.

D.H. Gordon and F.R. Nelson. Naval Hospital, Bethesda.

A chart format for compilation of data has been prepared by the associate investigator. Further investigation and recall of subjects already under study will await the return of the primary investigator on 31 Jan 1972.

CICC 2-06-319

TREATMENT OF TIBIAL STRESS FRACTURES WITH ELECTRIC MICROCURRENT. **S.H. James.**

Naval Hospital, Camp Pendleton.

Stress fractures of weight-bearing bones occur in about 4% of Navy and Marine trainees requiring several months to heal. This double blind study is designed to determine if ten microamperes of continuous electrical current delivered through a Kirschner wire cathode placed at the site of the stress fracture will significantly decrease healing time. Proposed study will include 15 patients and will commence in Jan 1972. Simultaneous studies using a common protocol will be conducted at Naval Hospitals San Diego and Beaufort.

M4305.05-3080AGG2

EVALUATION OF BICEPS CINEPLASTY. **L.H.**

Luppi and R.W. Gorski. Naval Hospital, Philadelphia.

The purpose of this investigation is to determine if the biceps cineplasty is more efficacious in the selected below-elbow amputee. Detailed questionnaires were sent to 33 amputees. Of these 33, 28 replied. All but two amputees were using the cineplasty prosthesis full time. In this preliminary investigation it was shown that the amputees with the cineplasty prostheses were using them as fully as the amputees with the conventional prostheses.

A further, more detailed report is pending.

MR041.20.01-0346A2GX

TREATMENT OF ANKLE FRACTURES. **A.M.**

Martinson and G.W. Cady. Naval Hospital, San Diego.

Three hundred twenty-seven ankle fractures admitted to Naval Hospital, San Diego, were reviewed in

order to formulate a concept of anatomic reduction and fixation. The distal tibiofibular angle was used as a guide to the adequacy of reduction. This angle is basically analogous to the axis of rotation of the tibiotalar joint and does not vary more than two degrees between the two ankles of a normal individual. Failure to restore the angle to normal following a fracture is usually due to persistent shortening or external rotation of the distal fibular fragment. This leads to abnormal biomechanical function of the joint and correlates well with less than optimal clinical results. Measurement of the angle is a simple method for judging the adequacy of reduction.

This study emphasizes the importance of the lateral malleolus in the treatment of ankle fractures and in the end results of that treatment.

M4305.05-3071AGG2

EVALUATION OF THE INCIDENCE OF CONGENITAL HIP DISEASE IN THE NEWBORN. **A.L. Rehme.** Naval Hospital, Jacksonville.

Evaluation of the incidence of potential congenital diseases in the newborn as detected by a positive Ortolani's sign is being conducted. An orthopedic surgeon examines infants within 24 hours after birth. All infants with a positive Ortolani's sign are treated with a modified Von Rosen splint. Follow-up X-ray studies are obtained at three, six, and twelve-month intervals.

Of the 1,038 infants examined since 1 April 1971, eight were detected with a positive Ortolani's sign. They were treated with a modified Von Rosen splint. Follow-up X-ray studies revealed normal hips.

The study thus far reveals an incidence of positive Ortolani's sign in approximately 1% of the newborns. It also indicates that when treated for the first three months of life, the infants will develop normal hips. The initial examining pediatrician, intern or resident failed to detect all but one of these cases.

CICC 2-8-523

EVALUATION OF CERVICAL SPINE INJURIES. **J.S. Romine; J.B. Oldershaw and D.C. Kaiser.** Naval Hospital, Great Lakes.

Ten patients with fractures of the cervical spine received 14 examinations under cineroentgenography performed between 1 Feb 1971 and 10 Jan 1972. All injuries had been treated with a period of immobilization for six to twelve weeks prior to examination. Seven of the fourteen studies were technically unsatisfactory. Two of the remaining seven studies led to the alteration of the plan of treatment with a resulting

change from a surgical to a conservative approach.

Four cases of previous cervical spine fracture, treated elsewhere, were examined in the standing position under the image intensifier, without cineroentgenography. Cervical biomechanics were more easily visualized in these cases than had been previously attained in the lying position necessarily imposed by the cineroentgen equipment.

CICC 2-13-004

SOFT TISSUE VARIABLES. **I.J. Woodstein.** Naval Hospital, Oakland.

This study seeks insight into patterns and magnitude of postsurgical changes in the amputation stump and development of criteria for more efficient determination of the optimum postoperative time at which to prescribe a permanent stump socket.

The method of volume determination makes use of a measuring chamber into which the stump is inserted. A nontoxic gas (carbon dioxide) is injected at a known rate into the chamber. As the gas is injected into the fixed volume of the chamber, the concentration level rises at a rate proportional to: the initial volume of the chamber, the gas injection rate, and the length of time the injection continues. Insertion of the amputation stump modifies the initial volume; by measuring the length of time required for the injected gas to reach a specific level, the volume of the stump may be deduced.

Installation of major subassemblies to the chassis has been accomplished and some of the electric circuits have been checked. Interconnecting wiring with disconnect plugs has been started. Redesign of the structure that maintains the shaft alignment has also been started.

MR041.20.01-0239A2GX

PLASTIC FOAM AS A PROSTHETIC STRUCTURE AND STUMP-FITTING MATERIAL. **I.J. Woodstein.** Naval Hospital, Oakland.

This study will investigate low exotherm, polyurethane foam for forming a stump socket directly on the amputation stump. Successful development may: (a) Promote rapid, inexpensive stump-socket fabrication; (b) Simplify many stump-fitting problems now existing, and (c) Provide substantial economies over present socket construction methods.

Proper metering to produce a consistent foam product and a containing technic to develop proper socket contours directly from the amputation stump under pressure developed by the foaming action, are being

developed. Our present special positive displacement dispensing machine shows promise but is not yet technically adequate.

Successful completion of the study may see the development of small aerosol packaging to promote rapid, individual and direct forming of the stump socket on the amputation stump.

MR041.20.01-0240A2GX

ARTICULATED FOOT/ANKLE ASSEMBLY. I.J.

Woodstein. Naval Hospital, Oakland.

Nationally, the most popular artificial foot features a solid ankle with cushioned heel construction which relies upon the resilience of its structure for mobility. We shall design an ankle/foot assembly to provide for natural motions of plantar and dorsal flexion, inversion and eversion and, most important, transverse rotation of the foot on the shin.

A major feature of the design will employ a flexible steel cable threaded through a bidurometer rubber bumper to provide natural mobility to the member, in addition to the advantages offered by a molded, flexible polyurethane foot.

Particular attention will be applied to cosmetic treatment of the junction between the foot and shin, and movement between these elements, because of the flexible cable substitution for the conventional rigid ankle bolt.

MR041.20.01-0344A2GX

ADVANCED DEVELOPMENT OF THE IMPROVED ORTHOPEDIC PRODUCTION TRIAD FOR CARE OF THE COMBAT CASUALTY. I.J. Woodstein. Naval Hospital, Oakland.

Now under development is a system of making, measuring, and finishing orthoses which combines a modular concept of fitting interrelated components to produce complete braces for individual patients, all accomplished in a central fabrication facility. Accomplishments to date include improved measuring/fabrication and finishing capabilities as applied to leg braces, plus an ability to transfer necessary data through an ordinary telephone. We are now building equipment to be used by another naval hospital to check out this part of our proposed system. With completion of this equipment, we hope to receive appropriate skiagraphs for use in producing the finished brace within a few hours. The finished brace will be forwarded to the requesting unit by air express, ready for the patient in less than 24 hours.

We feel we can surmount the several remaining technical problems to permit central fabrication of braces in the immediate future. Artificial limbs will be similarly fabricated at a later date. It will be feasible to centrally fabricate all braces required by the military within five years, for the western half of the U.S. Four additional years will probably be required to establish two additional centers for the eastern U.S.

M4305.05-3018AGG2

PLASTIC FOAM AS AN ORTHOPEDIC SPLINT FOR COMBAT CASUALTIES. I.J. Woodstein. Naval Hospital, Oakland.

It is planned to use a low-density, low exotherm, rigid polyurethane foam, developed in another Work Unit, as an experimental body-splinting material with the same function as plaster of Paris casts. This study will explore: formulations, appropriate cloth materials, packaging/dispensing of the foam materials, and particular studies of field applications.

When deposited between two layers of stockinet or cloth, a rigid, light-weight structure in "sandwich" form is produced, and may be manipulated by hand for a controllable period of time before polymerization occurs. Compared with plaster, the plastic foam is extremely light in weight.

M4305.05-3019AGG2

SILASTIC BONE CAP IMPLANT. I.J. Woodstein. Naval Hospital, Oakland.

This study will investigate the effect upon heterotopic bone formation at amputation sites, the use of "Silastic" bone caps.

Three implants have been locally performed and follow-up is being conducted. Photographic documentation of technics and progress of patients is being accomplished on a planned basis. If successful, the study may prevent bony overgrowth in juvenile amputees and further application may result in the use of such caps in below-elbow amputations to prevent undue cross scar formation between radius and ulna. This would conserve powers of pronation-supination that are now frequently lost.

This study is being conducted in cooperation with Dr. Ralph Lusskin at New York University, under Grant No. 2229-M from the Social and Rehabilitation Service of the Department of Health, Education and Welfare.

M4305.05-3057AGG2

ADJUSTABLE SOCKET. I.J. Woodstein. Naval Hospital, Oakland.

Present amputation stump sockets are rigid and maintain a fixed shape, while the stump tissues vary in size and contour for some weeks following amputation surgery. Maintenance of fit is now accomplished by replacing the sockets, several of which are required before the permanent socket is attained.

This study will employ a stack of thin metal sheaves, bolted together at their center points so that they may be spread out into a disc shape. The sheaves will then be shaped upward and around the amputation stump, where they will be held in place by an elastic bandage. The experimental socket is expected to serve in place of multiple early sockets, until the permanent socket is prescribed.

M4305.05-3060AGG2

ADJUSTABLE TOE PICK-UP BRACE. I.J. Woodstein. Naval Hospital, Oakland.

Spring braces designed to provide toe pick-up do not allow proper exercise of muscles following peripheral nerve injury.

We propose an adjustable mechanism to permit graded and predetermined decreases in the spring-assist function, so that the muscles can be more effectively exercised. Elastomeric or mechanical springs are planned to furnish the toe pick-up force and will be anchored by an adjustable method to permit variation in the force as required by the patient's condition.

M4305.05-3061AGG2

ADVANCED MEASUREMENT AND FABRICATION OF ORTHESES FOR THE COMBAT CASUALTY.

I.J. Woodstein. Naval Hospital, Oakland.

This study will seek to establish procedures for the central processing of completely prefabricated orthotic devices, based upon measurements and judgments of a qualified technician at a remote location. Savings in time, labor and materials are envisioned. Evaluation of data transmission systems, and the input terminal requirements needed to best serve the patient, shall be performed.

With successful completion of these trials, remote input centers will be designated and the necessary data links established between remote centers and the central processor. Continued development will be conducted to allow upgrading of technic so that prosthetic as well as orthotic devices may be produced.

M4305.05-3063AGG2

DISTAL PROSTHETIC SOCKET PAD. I.J. Woodstein. Naval Hospital, Oakland.

For several months following the initial fitting of the amputee, stump tissues shrink and undergo other changes. The stump tissues pull away from their intended partial-end bearing until such time as a new socket can be fitted.

The socket pad utilizes the unique qualities of polysiloxane ("silly putty") in which, when placed in the distal end of the socket, the stump forces the material to conform to the stump irregularities and thus restore end bearing. This increase in the modulus of rigidity, as the rate of shear increases, is a characteristic expected to extend the useful life of stump sockets. A by-product of the project may be a formerly untapped method of suspension.

M4305.05-3076AGG2

OTOLARYNGOLOGY

THE MEASUREMENT OF EUSTACHIAN TUBE FUNCTION USING TANTALUM POWDER. L.

Bowers; S. Weber and R.W. Cantrell. Naval Hospital, San Diego.

The purpose of this study is to obtain an accurate and useful clinical method to measure Eustachian tube function, since none exists at present time.

Tantalum powder will be placed in the mesotympanum of dogs and its clearance will be followed by temporal bone X-ray studies. Histologic sections of the middle ear mucosa will be taken to see if there is any reaction of the host tissue to the powder.

CICC 2-16-411

A STUDY OF ANATOMIC CHANGES IN THE MIDDLE EAR ASSOCIATED WITH NOISE-INDUCED HEARING LOSS AND ACOUSTIC TRAUMA. M.J.

Rensink; T. Acomb; S. Weber and R.W. Cantrell. Naval Hospital, San Diego.

The technical objective of this study is to correlate anatomic changes with noise-induced hearing loss and acoustic trauma. The histologic examination of temporal bones obtained from autopsies will be evaluated for changes in the auditory nerve and organ of Corti. Correlation will be made with the background of noise and acoustic trauma, as well as with clinical findings, including the audiogram, in active duty and retired personnel.

A temporal bone lab with a full-time technician trained in the Stacey-Guild technique for fixing, decalcifying, sectioning and staining of the bones, is being established.

MR041.20.01-0391A2GI

PATHOLOGY

ROUTINE HISTOLOGIC EXAMINATION OF EYES IN MILITARY PERSONNEL AT AUTOPSY. B.R. Blais and C.F. Bishop. Naval Hospital, San Diego.

Information in ophthalmic pathology, with clinical pathological correlation, will be gained from the study of eyes at the time of autopsy. This will permit a correlation between the ophthalmic pathology findings and the other general pathologic changes noted as part of the routine autopsy protocol. Much information on ocular pathology in postmortem patients is needed. CICC 2-16-425

PATIENT CARE

SCREENING FOR KIDNEY DISEASE IN RECRUITS. L.G. Dickson. Naval Medical Research Institute (NMRI), National Naval Medical Center (NNMC), Bethesda.

The goal has been the application of selected screening tests for the detection of occult parenchymal kidney disease and urinary tract infection. Currently first-enlistment incidence of kidney disease is 199/100,000 population, with average hospitalization of eleven days. For urinary tract infection the incidence is 136/100,000 population, with average hospitalization of 6.6 days. These morbidity figures do not include outpatient care nor hospital admissions for "symptoms" such as hematuria or albuminuria where no underlying disease is detected. Suitable screening tests would reduce the above morbidity and associated expense.

Single random sample tests of blood and urine have been evaluated including: blood urea nitrogen (BUN), serum sulfate, creatinine and bacterial metabolites. None has proven to be more reliable than a carefully performed urinalysis including the microscopic examination. In fact, the BUN, sulfate and creatinine determinations have proven to be abnormal in 5, 15 and 9 percent, respectively, of patients with urinalyses containing evidence of renal disease. Biochemical evidence

of infection has been present in only 45% of specimens containing greater than 100,000 organisms per ml, as determined by standard cultural techniques.

Rapid inexpensive bacteriologic cultural methods are now under test for suitability to detect occult urinary tract infection.

M4305.05-3055AGG2

USE OF PARAMEDICAL PERSONNEL TO PERFORM ROUTINE MEDICAL DUTIES ON MILITARY PERSONNEL AND DEPENDENTS. C.C. Scott, III; R.F. Kirk and J.A. Zimble. Naval Hospital, Philadelphia.

The purpose of this study is to evaluate the acceptance and feasibility of using "on the job"-trained females as paramedical personnel in Obstetrics and Gynecology.

Out of approximately 25 applicants, a 29-year-old Registered Nurse was selected to participate in this study.

Due to the short period of time which has elapsed, no conclusion is possible at this time.

CICC 2-05-604

PEDIATRICS

A PROSPECTIVE COOPERATIVE STUDY OF THE ETIOLOGY OF REYE'S SYNDROME AND THE EFFECTIVENESS OF CURRENT MODES OF THERAPY. M.N. Goldschmidt and D.W. Bailey. Naval Hospital, Bethesda.

Multiple retrospective reports or brief case histories form the bulk of the data on Reye's Syndrome of fatty degeneration of the viscera with hepatic encephalopathy.

A prospective study involving 26 of the major graduate training hospitals of the United States Navy, Army, and Air Force will investigate possible etiologies, prognostic guidelines, and effectiveness of conservative therapy in this disease.

In a second phase of this study, one of the newer therapies will be compared with basic conservative therapy. Epidemiologic studies will be performed by the Center for Disease Control.

CICC 2-06-336A

EFFECT OF EARLY HYDRATION ON SERUM BILIRUBIN. **W.L. McLean and T.J. Williams.** Naval Hospital, Boston.

A significant number of newborns who are breast-fed develop nonhemolytic jaundice and are at risk of neurologic damage. The purpose of this study is to determine the effect of early hydration of the breast-fed infant with supplemental glucose and water.

A control (nonsupplemented) and study group (hydrated) of breast-fed babies, selected randomly, are followed by daily measurements of serum bilirubin, hematocrit and total serum solids to assess the effect of hydration via physical parameters. Neurologic examination and mental development assessment will be done at three, six and twelve months, and will be correlated with nursery findings. Because of the long-term nature of the study, insufficient data is available to draw any conclusions at this time.

CICC 2-02-110

PSYCHIATRY

METHODS FOR EVALUATING AND TREATING PSYCHIATRIC DISORDERS. **B.C. Becker; N.**

Weinberg and L. Acord. Naval Hospital, Bethesda.

A variety of studies are in progress and represent parts of this project.

One study on sensitivity training for Neuropsychiatric (NP) Technicians found that considerable structure and more direct empathy training seemed more effective than sensitivity groups. Individual outcomes were related to individual expectations.

A second study is in progress, comparing subtest patterns on intelligence quotient (IQ) tests at intervals following head injury to test-retest results on normals.

A third study found deficit in higher cognitive functions following repeated use of hallucinogenic drugs.

A fourth study in progress explores this deficit in more detail, using factor-analytic procedures.

MR041.20.01-0140A2AF

PSYCHOLOGICAL MASTERY OF VISUAL TRAUMA. **M.J. Horowitz; P.T. Malone and E.J. Voltolina.** Naval Hospital, Oakland.

Behavioral responses to external stress, such as decompensation in combat, are due to cognitive mediation. The present studies are part of experimental investigations of cognitive response to psychological stress.

The method of creating a stressful situation is the use of stressful motion pictures. Cognitive responses are assessed, using self-reports and content analysis of reports of mental contents, during a variety of tasks which include an auditory signal detection task. Subjects have been selected from normal control groups, as well as psychiatric patients with nonpsychotic types of psychiatric disorders.

Both types of subject groups have been found to exhibit significant increases in intrusive and repetitive thinking after stress events, as induced by stressful films. Those persons who report the highest levels of emotional stress tend to be those persons who are found to have the greatest increase in intrusive and repetitive thought after stress. Psychiatric patients tend to report less thought in general than nonpsychiatric patients. When data is transgenerated yielding the number of intrusions and the number of repetitive thoughts per 100 words, then psychiatric patients are found to exhibit significantly higher levels of intrusive and repetitive thinking after stress than do nonpatient controls. The findings of increased intrusive and repetitive thought after stress do not correlate with decrements in task performance in the signal detection task. The psychiatric patients do not differ from the nonpatient controls in their task performance.

MR005.20.01-0221A2HX

TREATMENT STRATEGIES FOR PSYCHIATRIC PATIENTS ON ACTIVE DUTY IN THE NAVAL SERVICE. **R.E. Strange; E.K.E. Gunderson and D.E. Brown.** Naval Hospital, Philadelphia.

In order to assess treatment programs and study emotional problems impairing effectiveness of Navy-Marine Corps personnel, clinical data about patients hospitalized in the Navy East Coast Neuropsychiatric Treatment Center, Philadelphia, is continuously recorded and reviewed. Strategies of treatment, events of hospitalization, and administrative-dispositional data are simultaneously recorded for correlation. Significant factors in staff attitudes and treatment methods have been identified and studied, as well as specific aspects of common military problems including emotional adjustment following combat experience and isolated duty, drug and alcohol abuse, and violence.

Data is currently undergoing specific review for special studies of participants in the Navy-Marine Corps exemption program for drug abuse, patients in disciplinary status, and alcohol problems.

M4305.07-3006BGB5

PULMONARY DISEASE

A STUDY OF THE BACTERIAL CONTAMINATION OF HUMIDIFIED GAS IN A RESPIRATORY INTENSIVE CARE UNIT. **S.M. Bowles and D. Schubert.**

Naval Hospital, Portsmouth, Va.

The purpose of the study is to quantitate the contribution of contaminated wall gas and entrained room air to hospital-acquired respiratory infections. The effectiveness of presently available devices for filtering humidified gas will be tested.

To date, only preliminary studies have been done. These studies reveal that wall gas is contaminated and entrainment of room air increases the contamination of humidified gas.

CICC 2-08-503

LUNG PATHOPHYSIOLOGY AND ITS RELATION TO THE CLINICAL SPECTRUM OF THE FAT EMBOLISM SYNDROME. **S.M. Bowles; S. Loxley; C.S. Lambdin and B.L. Aaron.**

Naval Hospital, Portsmouth, Va.

The purpose of the study is to determine the incidence, natural history, and exact nature of pulmonary abnormalities associated with fracture of the lower extremities. Attempts to identify the etiology of these abnormalities will be made.

To date, ten patients have been studied. Five of these have experienced a transient drop in PaO_2 (partial pressure of oxygen in arterial blood) of 20 to 50 torr (pressure of 1 mm Hg at 0°C and standard gravity) while breathing room air. There has been only one patient that exhibited classic symptoms of fat embolism. Another patient studied 12 hours postinjury had a PaO_2 of 44 torr while breathing room air. He had no symptoms and his PaO_2 was stable in the 40 to 50 range while breathing air for two weeks. Pulmonary abnormalities have reappeared in two patients when they had surgery at a later date. All patients exhibiting hypoxemia were treated with O_2 alone. A-a O_2 (alveolar-arterial oxygen tension gradient) gradients range from 200 to 450 torr in those patients hypoxic while breathing air. There was no predictable pattern in physiologic dead space to tidal volume ratio.

Lipid and clotting studies have been obtained but no conclusion about them is possible at present. More sophisticated additional pulmonary studies are planned to define the exact nature of the abnormalities.

The incidence of hypoxemia after lower extremity fractures is high and mostly unrecognized. Admission and daily blood gas studies should be a routine part of the care of these patients.

CICC 2-08-504

PULMONARY FUNCTION SCREENING BY FLOW-VOLUME LOOP ANALYSIS. **H.N. Dean; L.A. Sheffer and J.L. Steffenson.**

Our objective is to demonstrate the usefulness of flow-volume loop analysis as a screening tool to prevent the induction into military service of men with undetected pulmonary disease.

Unselected inductees undergoing physical examination will be tested on a flow-volume loop system. The operator will make a permanent recording of any abnormal loop by means of photography. These individuals will then be referred to the Nav Hosp Oakland, for a thorough evaluation including blood gas analysis, chest X-ray, and pulmonary function testing (PFT).

Currently our loop system is being compared to routine PFT methods to demonstrate its reliability.

Though incomplete, early results indicate it should have acceptable accuracy and precision. It is estimated that approximately four months will be needed to finish calibration of normal loops.

MR005.20.01-0336A2HX

THE CLINICAL EFFICACY OF COMBINED "NON-SURGICAL" BIOPSY PROCEDURES IN THE DIAGNOSIS OF INTRATHORACIC LESIONS. **R.C. Elliott; J.F. Smiddy and D.W. Shea.**

This is a prospective study evaluating the efficacy of the concurrent use of all accepted "nonsurgical" biopsy procedures for intrathoracic lesions. The techniques being studied include transthoracic needle aspiration and/or percutaneous puncture biopsy under guidance of biplane fluoroscopy, and transnasal fiberoptic bronchoscopy.

Eighty patients have been studied to date with transnasal fiberoptic bronchoscopy. This has proven to be an excitingly new and enlightening procedure. It is well tolerated by the patients and allows clear visualization through the level of the tertiary bronchi. Due to the tenfold magnification, lesions in the subsegmental bronchi can be clearly visualized and photographed, and biopsies may be obtained under direct visual control.

It is anticipated that the versatile diagnostic capabilities of this instrument far outstrip those of the standard straight metal bronchoscope.
CICC 2-06-305

EVALUATION OF BRONCHIAL BRUSHING IN CHEST DIAGNOSIS. R.G. Fosburg; J.A. Gibbons and T.L. Folkerth. Naval Hospital, San Diego.

Reports of bronchial brushing techniques have indicated significantly higher diagnostic yields in patients with peripheral pulmonary lesions as compared to diagnosis obtained by analysis of sputa and standard bronchoscopic studies.

Preliminary clinical trials of bronchial brushing suggest that localization by biplane fluoroscopy and/or flexible fiber bronchoscopy are essential if optimal results are to be realized from this procedure. Experience in twelve clinical cases employing the Medi-Tech (R) catheter brush system through a rigid bronchoscope and single-plane image intensification yielded a diagnosis with this modality in only one case.
CICC 2-16-412

EVALUATION OF TREATMENT OF PULMONARY DYSFUNCTION FOLLOWING HEMORRHAGIC SHOCK. R.G. Fosburg and R.W. Virgilio. Naval Hospital, San Diego.

In order that effective research on the pathophysiology of posttraumatic pulmonary insufficiency may be performed, we must establish an effective monitoring system for the patient in acute respiratory failure. Our present research has been limited by the inability to easily measure on-line the mechanics of respiration, and by the arduous, time-consuming hand calculation of data.

Automated techniques are available through the University of California, San Diego (UCSD) patient-monitoring project for the testing of respiratory function in the critically-ill patient. These techniques could be made available to the shock research unit at the Naval Hospital, thereby providing a badly needed on-line analysis of respiratory function in our critically-ill patients. This will be accomplished by transmission of data over two flowmeter lines and one slow-speed line from a special bedside respiratory cart to the UCSD patient-monitoring project computer.
MR041.20.01-0289A2GX

EVALUATION OF PULMONARY EMBOLI AS THE PATHOPHYSIOLOGIC MECHANISM OF PULMONARY DAMAGE AFTER TRAUMATIC INJURY. J.W. Hammon, Jr.; M.J. O'Sullivan; J.E. Lang and R.G. Fosburg. Naval Hospital, San Diego.

Pulmonary thrombi have been shown to be present in patients' lungs after severe trauma. The mechanism of pulmonary damage is unclear, but the liberation of neurohumoral agents from thrombi is suspected.

Canines will have their lungs denervated by autotransplantation to abolish pulmonary reflexes. Autologous thrombi will be formed by injection of concentrated factor VII solution. The concentration of neurohumoral agents, i.e., serotonin, histamine and fibrin degradation products, will be measured across the lung. The response of the denervated lung will be evaluated in the light of possible neurohumoral release.

Preliminary results show a significant increase of serotonin and fibrin degradation products in pulmonary venous blood after embolization.
M4305.05-3072AGJ2

MEASUREMENT OF CHANGE IN WORK OF BREATHING IN HUMANS WITH RESPIRATORY FAILURE DURING WEANING. E.R. Lucier and J.J. Angel. Naval Hospital, Great Lakes.

The indirect measurement of the change in work of breathing by oxygen consumption measurements was determined by the use of a modified basal metabolic rate (BMR) machine in patients recovering from respiratory failure at the time of weaning.

All of the patients measured so far have shown either no change, or a slight decrease in oxygen consumption when changing from controlled to spontaneous ventilation.
CICC 2-13-012

PHYSIOLOGIC INDICATORS OF STEROID THERAPY IN PULMONARY SARCOIDOSIS. D. Reid. Naval Hospital, San Diego.

This study is designed to take a look at a number of pulmonary physiologic parameters which, hopefully, will provide an index for steroid therapy in patients with pulmonary sarcoidosis. Those parameters being measured presently are: (1) static and dynamic volumes; (2) diffusion capacity of the lungs, resting and exercise and dead space to tidal volumes ratio.
CICC 2-16-428

CARE OF NAVAL AND MARINE CASUALTIES — PHYSIOLOGIC STUDIES IN SPONTANEOUS PNEUMOTHORAX. J.V. Scutero. Naval Hospital, Portsmouth, Va.

The alterations in cardiopulmonary physiology induced by spontaneous pneumothorax in subjects without prior evidence of cardiopulmonary disease will be evaluated.

Patients with spontaneous pneumothorax will have arterial blood gases performed prior and subsequent to definitive therapeutic intervention. These studies will be accompanied by serial electrocardiograms and chest X-ray assessments. The radiographic estimation of percent pneumothorax will be correlated with the value obtained by direct measurement of the air aspirated, and complete ventilatory studies performed following reexpansion.

Due to continuing problems with the functioning of the plethysmograph, no patients have been studied as yet. However, these studies will commence shortly. MR005.20.01-0273A2HX

SHIPBOARD ISONIAZID CHEMOPROPHYLLAXIS IN MICROEPIDEMICS OF TUBERCULOSIS. J.V.

Scutero, R.S. Lisella and E.J. Clarke. Naval Hospital, Portsmouth, Va.

The efficacy of the immediate institution of isoniazid chemoprophylaxis in the prevention of tuberculous infection in shipboard environments following the initial detection of an active case of pulmonary tuberculosis will be evaluated.

Initially, a ship's complement, amongst whom an active case of pulmonary tuberculosis has been identified, will be investigated in accordance with the current instruction on tuberculosis control. Tuberculin conversion rates over the ensuing twelve-month period will be carefully tabulated as regards percentage of ship's complement and time of conversion. All personnel transferred to the ship after detection of the source case will be included in the study. A ship of similar design and size of complement will be investigated when a case of active pulmonary tuberculosis has been identified. However, all members of the crew will receive isoniazid (INH) chemoprophylaxis from the onset for six months. Conversion rates and time of conversion will be statistically compared to validate the contention that INH chemoprophylaxis will reduce shipboard tuberculous infection.

To date no case of active tuberculosis has been identified on a ship of similar size and complement to the initial ship studied (USS AMPHION). This will be necessary for completion of the study.

MR041.20.01-0322A2GX

OCCULT OBSTRUCTIVE AIRWAY DISEASE. J.V. Scutero and H.R. Maxon. Naval Hospital, Portsmouth, Va.

Chronic obstructive pulmonary disease represents a significant impediment to the performance of duty by active duty military personnel, particularly in the spheres of aviation and submarine medicine. Present physiologic standards establish a diagnosis only when significant impairment is present. Accordingly, it is proposed that an abnormally-increased functional residual capacity (FRC), in the presence of an otherwise normal pulmonary function assessment, is sufficient evidence to document the presence of chronic obstructive pulmonary disease.

Symptomatic or asymptomatic personnel with normal chest X-ray and pulmonary function studies except for an increased FRC, will undergo sophisticated physiologic studies to document the presence of obstructive pulmonary disease. Individuals with chronic bronchitis and asthma will be excluded. Studies will include: arterial blood gas analysis, diffusion capacity, compliance, airway conductance and radioactive Xenon-133 ventilation/perfusion scans.

We are awaiting the purchase of necessary equipment to begin this study.

MR041.20.01-0334A2GX

EFFECT OF CHEST PHYSIOTHERAPY ON PULMONARY GAS EXCHANGE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

D.W. Shea and R.C. Elliott. Naval Hospital, Bethesda.

In most hospitals much time is devoted to chest physiotherapy in the patient with chronic obstructive pulmonary disease (COPD). Previous published studies have shown no significant posttreatment improvement in flow rates or sputum production.

This is a prospective study of the efficacy of chest physiotherapy as measured by changes in Alveolar-arterial oxygen (A-a) gradients, ratio of physiologic dead space to tidal volume (VD/vt), and diffusion of carbon monoxide (DL_{CO}). A preliminary study of four patients with COPD has revealed a significant improvement in the A-a gradients and VD/vt ratio after chest

therapy. It is anticipated that chest physiotherapy will improve DL_{CO} in such patients.
CICC 2-06-307

RADIOLOGY

DIAGNOSIS OF MULTIPLE SMALL PULMONARY EMBOLI WITH ^{99m}Tc MICROSPHERES. L.L. Heck; W.M. Beckner and J. Duley. Naval Hospital, Bethesda.

The purpose of this study is to improve the recognition of multiple small pulmonary emboli which frequently go undetected by current clinical and radiologic studies.

Dogs and rats will be embolized through the pulmonary artery with controlled numbers of lead beads ranging in size from 100 micra to 5 mm. The animals will then be injected with ^{99m}Tc (technetium) microspheres for perfusion lung scans. We will then evaluate the degree of pulmonary arteriovenous shunting of the microspheres by quantitating the radioactivity of other body organs.

Studies have shown that anatomic pulmonary arteriovenous anastomoses up to 100 micra in diameter are present. It is postulated that these anastomoses may become functional in the presence of multiple small emboli or acute or chronic pulmonary hypertension. The 15-30 micra diameter albumin microspheres which we use for clinical lung scanning would readily shunt through these anastomoses.

We have encountered a few patients with proven pulmonary emboli who have abnormally increased levels of radioactivity in the brain after routine lung scans. This would indicate that there are significant pulmonary to systemic vascular shunts in these patients. Currently we are utilizing a videotape data-processing system to quantitate cerebral radioactivity before and after microsphere injection for lung scanning. Improved methods for geometric correction of counts obtained must be developed before this method can become clinically useful.

MR041.20.01-0281AWHX

EVALUATION OF TIME-SAVING POTENTIAL OF PERSISTENCE SCOPE. C.P. Myers. Naval Hospital, Great Lakes.

The time required to perform a radioisotope study with an Anger gamma camera is dependent on the time required to properly position the patient in respect to the camera, and hence, on the technician's ability to

visualize the organ being imaged during the positioning process. This time is analyzed by alternately performing identical studies with and without a persistence scope to enhance visualization of the imaged organ, especially in studies where the count rate is so low that the statistical randomness of the photons detected masks the image on the normal cathode-ray display.

The persistence scope was received and installed in mid-December. However, the amount of data obtained is statistically insufficient to draw any conclusions at this time.

CICC 2-13-016

EVALUATION OF RADIOIMMUNOASSAY KITS.

G.J. Weir, Jr. (With technical assistance from J.W. Reed). Naval Hospital, Great Lakes.

Total serum thyroxine levels and T_3 (triiodothyronine) resin uptakes provide a measure of thyroid function but both are affected by the level of thyroid-binding protein. A recently developed method of experimentally determining the relative level of free thyroid hormone, (RES-O-MAT ETR Diagnostic Test, Mallinckrodt Nuclear) has been evaluated.

The coefficient of variation for this test on duplicate pooled serum samples was 1.7%. For T_4 level determinations, it was 1.9% and for T_3 resin uptake, 2.2%. Using a control abnormal serum values were 1.1, 1.8 and 1.8%, respectively. The experimental thyroxine ratio correctly placed 36 of 36 euthyroid, 3 of 3 hypothyroid and 6 of 7 hyperthyroid patients. The T_4 level was "correct" in 27 of 36 euthyroid, 7 of 7 hyperthyroid and 2 of 3 hypothyroid patients. The T_3 resin uptake was "correct" in 31 of 34 euthyroid, 5 of 7 hyperthyroid and 1 of 3 hypothyroid patients. Mathematical calculation of an index of free thyroxine level was correct in 33 of 34 euthyroid, 7 of 7 hyperthyroid and 2 of 3 hypothyroid patients.

The experimental determination of free thyroxine is thus as reproducible as the T_4 level and T_3 resin uptake and correctly distinguishes thyroid status in patients on drugs and with illnesses which affect the other determinations. It proved as effective as the mathematical index of free thyroxine in diagnosis, and is more easily performed than the dual determination of T_4 level and T_3 resin uptake.

CICC 2-13-006

RADIOISOTOPIC DETERMINATION OF GLOMERULAR FILTRATION RATE (GFR) AND EFFECTIVE RENAL PLASMA FLOW (ERPF). G.J. Weir, Jr. Naval Hospital, Great Lakes.

Determination of ERPF has not become a common clinical aid because of the difficulty of chemical determinations of para-aminohippuran. Clinical GFR determinations are approximated by creatinine clearance because of similar problems with inulin. This necessitates 24-hour urine collections, an error-prone procedure.

A technique has been developed which permits determination of ERPF and GFR, alone or simultaneously, from the plasma disappearance curves of radioactive compounds. No urine collections are necessary. A single injection of the radioactive compound is utilized. Determinations require approximately two hours of patient time and six blood samples at specified times following injection.

Using this technique 25 measurements were made on 17 normal people. ERPF was 561 ± 115 ml/min (mean \pm standard deviations), GFR 190 ± 47 ml/min (both values corrected to 173 m^2 body surface area).

CICC 2-13-009

THE ROLE OF THYROTROPIC HORMONE (TSH) IN SIMPLE AND MULTINODULAR GOITER AND IN THYROID CARCINOMA. G.J. Weir, Jr. and R.W.

Spath. Naval Hospital, Great Lakes.

A radioimmunoassay for TSH is being developed and will be used to evaluate the role of TSH in the pathogenesis of goiter and to evaluate the efficacy of thyroid replacement therapy.

Arrangements have been completed for the principal investigator and a technician to learn the technique of TSH radioimmunoassay at a laboratory currently performing the study. Serum samples from patients with goiter and thyrotoxicosis have been saved for future analysis.

CICC 2-13-013

DIAGNOSIS OF EARLY ARTHRITIS BY JOINT SCINTIPHOTOGRAPHY. G.J. Weir, Jr. and R.H.

Easterday. Naval Hospital, Great Lakes.

Joint scintiphotography $^{99\text{m}}$ Tc-technetium pertechnetate demonstrates nonspecific abnormalities in joints involved with arthritic conditions. The pattern of joint scintiphotography in early arthritis is being evaluated.

Studies of normal joints in patients undergoing brain scanning reveals a pattern of relative lack of activity in

the proximal palm and in the knee joint region immediately following injection of pertechnetate. At 30 minutes postinjection the pattern of activity is more homogeneous.

CICC 2-13-014

DIAGNOSIS OF URINARY TRACT OBSTRUCTION BY SCINTIPHOTOGRAPHY. G.J. Weir, Jr.; K.R.

Hutchins and J.E. Keeton. Naval Hospital, Great Lakes.

The possibility of diagnosing and localizing urinary tract obstruction by scintiphotography, especially using newer agents with high photon flux is being evaluated.

Scintiphotographs of the kidneys are obtained for up to two hours following the injection of ^{131}I -Hippuran and/or $^{99\text{m}}$ Tc-iron ascorbate acid complex. The scintiphotographs are evaluated without knowledge of the clinical status of the patient. In addition to routine scintiphotography, a Super-8 movie camera is being evaluated as a recording medium. Two patients have been studied to date. In one a ureteropelvic junction obstruction was correctly diagnosed from routine Polaroid scintiphotos. Renography and renal scintiphotography were normal on the second patient. Intravenous pyelography was also normal and the final diagnosis excluded urinary tract obstruction.

CICC 2-13-017

DYNAMIC SCINTIPHOTOGRAPHY IN THE EVALUATION OF RENAL DISEASE. G.J. Weir, Jr. Naval Hospital, Great Lakes.

Dynamic scintiphotography using a variety of radio-nuclides including $^{99\text{m}}$ Technetium pertechnetate, ^{131}I -Hippuran and $^{99\text{m}}$ Tc-iron ascorbate complex may be of value in differentiating renal cysts and tumors and in evaluating renal parenchymal disease. Studies are being performed using a persistence scope attachment to the gamma camera and 8-mm film. The equipment has just been installed.

In one patient studied using routine scintiphotography an inflammatory mass was present as an area of decreased activity using both ^{131}I -Hippuran and the $^{99\text{m}}$ Tc-iron ascorbate complex.

CICC 2-13-018

SURGERY — GENERAL

CALIBRATED OCULAR PLETHYSMOGRAPHY IN THE EVALUATION OF INTERNAL CAROTID FLOW.

W. Gee and H.W. Eisenberg. Naval Hospital, St. Albans.

For improved monitoring of cerebral blood flow in the casualty undergoing operation for carotid artery injury or brain trauma, calibrated ocular plethysmography is being evaluated.

A plastic cup, originally designed for use in suction ophthalmodynamometry, is connected to a specially constructed volume transducer with thick-walled vinyl tubing. The cup is applied to the sclera lateral to the limbus, and 50 mm Hg suction is applied to the closed system. Slight distortion of the globe is created. Each pulse wave entering the globe enlarges the globe slightly, and this enlargement decreases the curvature of any given arc of the sphere. Therefore, the area of the sphere under the cup is withdrawn slightly, causing a decrease in volume and an increase in negative pressure (suction) within the closed system. By using differential chambers in the transducer, the pressure change is minimized and the volume change is maximized. Connected to the closed system by a sidearm is a 1.0 mm³ calibration chamber, the introduction of which permits accurate adjustment of electronic gain. Calibration is essential for the comparison of studies done on different patients or for comparison of studies done on the same patient at different times.

The equipment has been applied in the research laboratory on dogs, during which the ipsilateral carotid artery has been temporarily occluded, followed by ligation, and finally by resection of the ligated portion and end-to-end anastomosis of the artery. Serial plethysmographs document, with remarkable accuracy, partial or complete occlusion and patency.

MR005.20.01-0262A2HX

EFFECTS OF INTRAVENOUS POTASSIUM IN POST-OPERATIVE PATIENTS. **L.C. Getzen and R.C.**

Laning. Naval Hospital, San Diego.

Animal studies were completed using four intravenous fluid regimens in the treatment of acute, severe hemorrhage. The use of potassium with a protein-containing solution resulted in a better survival with prolonged resuscitation. The serum albumin remained elevated above normal for one week when potassium was used. There were no adverse effects with the infusion of a potassium-containing fluid during resuscitation. There appears to be a significant reduction in the quantity of fluid required for resuscitation when

protein and potassium are administered concurrently. If this is true, the use of frozen blood in acute casualties would be practical. There were no cardiopulmonary complications in these animals.

MR041.20.01-0254A2GX

THE TREATMENT OF THERMAL BURNS WITH HYPERBARIC OXYGEN: A RETROSPECTIVE STUDY. **G.B. Hart; R.E. Thompson and F.L.**

Depenbusch. Naval Hospital, Long Beach.

Twenty-four patients with burns covering 20-50% of total body surface (TBSB), with 10% full thickness defects, were treated with hyperbaric oxygen (OHP) from 1 Jul 1969 to 1 Jul 1971. OHP schedule was 2 atm absolute oxygen 90 min. every 12 hours for one week, then 2 atm 2 hrs. daily until reepithelialization or grafting was completed.

These patients were compared with 28 patients treated without OHP from Feb 1967 to 1 Jul 1969. A 43% reduction in hospital stay and 25% reduction of predicted fluid requirements was observed in the OHP group. A randomized double-blind series is in progress.

M4306.01-3035AGG2

SKIN PREPARATION FOR SURGERY. **C.H. Lowery and M.L. Hawkins.** Naval Hospital, Portsmouth, Va.

This study will compare the use of a standard ten-minute preoperative skin scrub with the simple application of an antiseptic solution.

Patients undergoing indirect inguinal hernioplasty, who are otherwise free of local and systemic disease, will be randomly assigned to two groups: one receives a standard ten-minute preoperative scrub using Betadine soap, followed by Betadine antiseptic solution; the other group receives only Betadine spray. All patients will be shaved and prepped by the same corpsman. Patients will have serial skin cultures preoperatively, intraoperatively, and postoperatively using control culture plates for bacterial identification and colony count. Any wound infection will be correlated to the type of wound preparation, if possible.

This project is currently in progress, and to date, there is no noticeable difference in the bacterial species or colony count between the two groups. There have been no wound infections in either group.

MR041.20.01-0331A2GX

RESEARCH LABORATORY. R.L. Mullin. Naval Hospital, Boston.

The provision of research space, associated personnel and minor supplies by the Research Laboratory has allowed many physicians at Naval Hospital Boston to pursue their professional interests. Surgical residents have had the opportunity to develop surgical techniques in the canine laboratory. Postoperative ventilatory function has been investigated in both clinical and laboratory situations. Cardiac output determinations have been performed in the laboratory prior to use on a clinical basis. Electromagnetic flowmeters are being evaluated. Muscle pH in ischemic extremities is under investigation.

CICC 2-02-105

HYPERALIMENTATION AS A MEANS OF ESTABLISHING IMPROVED PREOPERATIVE NUTRITIONAL STATUS IN SELECTED PATIENTS. D.W. Oller. Naval Hospital, Bethesda.

This study is evaluating the benefit of intravenous hyperalimentation to seriously ill preoperative patients. Standard technics of intravenous alimentation are used while nitrogen balance studies are performed.

Preliminary studies show hyperalimented patients to be better operative risks, with decreased morbidity and decreased hospitalization time.

CICC 2-06-306

COMPARISON OF L-ESSENTIAL AMINO ACIDS AND PROTEIN HYDROLYSATES IN PARENTERAL HYPERALIMENTATION. D.E. Smith and R.C.

Laning. Naval Hospital, San Diego.

Since the introduction of total and supplemental parenteral hyperalimentation by Dudrick in 1968, it has rapidly gained acceptance and is often the sole means of achieving adequate nutrition in seriously-ill surgical patients. However, the protein hydrolysates used in the original preparations contained large amounts of polypeptides which cause considerable reaction because of their antigenicity, particularly nausea and fever. These polypeptides are metabolically inactive and are excreted unchanged. This represents a significant loss of nitrogen. L-amino acids represent the ideal theoretical substitute for protein hydrolysate, but they have not previously been available because of their cost.

Abbott Laboratories have now developed a preparation of synthetic amino acids containing the eight essential and two nonessential amino acids. This solution has an additional advantage. It causes utilization

of urea to form nonessential amino acids, thus lowering BUN and making it suitable for uremic patients. Our evaluation will be part of the Abbott Laboratories' Phase III new drug application. As soon as this preparation becomes available in April 1972, it will be compared with our present hyperalimentation solution in alternate patients. Objective data including nitrogen balance, serum proteins, serum chemistries and weight gain, as well as clinical and subjective improvement, will be recorded. The differences in objective parameters will be subjected to statistical analysis.

MR005.20.01-0358A2GJ

SURGERY — ORAL

STUDY OF METAL IMPLANTS IN THE MANDIBLE. D.V. Castner and I.J. Weber, Jr. Naval Hospital, Camp Pendleton.

Metal supports that can serve as abutments for fixed and removable dentures are fabricated and set on and into the mandible. Anchorage points for bridges and dentures are made from cast surgical chrome cobalt alloy and are set into or on the mandible. Metal implants, both end-osseous and suprapariosteal, are well tolerated and adequately support bridges and dentures.

Both end-osseous and suprapariosteal metal implants serve as excellent, strong abutments for bridges and dentures and are practical.

MR041.20.02-0374 A3II

STUDY OF TREATMENT OF MIDDLE-THIRD FACIAL FRACTURES. D.V. Castner and W.W. Magnus. Naval Hospital, Camp Pendleton.

The various methods of treating fractures of the middle third of the face are being evaluated. The fractures are being treated by open (transoral and extra-oral) and closed methods, with and without transosseous wires.

Postoperative radiographic studies indicate that good access and visualization are necessary to properly treat these fractures. Best results are achieved in serious complicated injuries by combined transoral and extra-oral approaches with interosseous wiring.

MR041.20.02-0375A3II

EXTRACRANIAL SUSPENSION VS. INTRAOSSEOUS AND INTEROSSEOUS SUPPORT IN THE TREATMENT OF FACIAL FRACTURES. W.R. Hiatt, W.E. Sugg and E.L. Mosby.

Naval Hospital, San Diego.

Survival of patients with severe facial trauma is increasing due to rapid transportation and evacuation along with intensive therapy administered soon after injury. Because of these lifesaving methods, the practitioner is faced with increasingly complicated facial fractures.

Documentation and comparison of the many modalities in treatment of these injuries is under study from several clinical views.

CICC 2-16-416

MAXILLOFACIAL COMBAT CASUALTY REHABILITATION WITH BONE GRAFTS. H.J. Sazima; L. Gold and J.F. Kelly.

Naval Hospital, Philadelphia.

Traumatic acquired and/or congenital defects of the face, jaws, and/or associated structures are amenable to reconstruction if the missing osseous structures are replaced. To date autogenous osseous or particulate matter in a metal framework have been chiefly used. The basic work of Urist, Burwell and Boyne suggests a composite bone homograft may obviate the former techniques and the time-consuming, morbid, sometimes marginal esthetic and functional results.

Surface decalcified homografts augmented, treated, and sterilized by various methods, will be employed via trans- and extraoral approaches to replace facial and jaw bones, and eventually, the entire mandible and joints. Animal models will be developed to test the above hypothesis and evaluate composite homograft bone induction.

MR041.20.02-0388A3IE

SURGERY — PLASTIC

MAXILLOFACIAL DEFECT STUDY. G.W. Anastasi.

Naval Hospital, Boston.

The purpose of this study is to evaluate and treat maxillofacial defects both congenital and traumatic. The multidisciplinary approach is stressed in the management of these cases. Over 200 children have been registered in the Cleft Palate Clinic. Reconstructive problems associated with developmental palatal deformities are analogous to those seen in traumatic injuries of the palate. The correlation of these two areas has greatly aided in the understanding of the

problems associated with the reconstruction of both the congenital as well as traumatic maxillofacial defects.

Reconstructive surgery of maxillofacial defects with particular emphasis on restoration of function is the aim of the maxillofacial team. The team, comprised of a Plastic Surgeon, Otolaryngologist, Pediatrician, Speech Pathologist, Oral Surgeon, Orthodontist and Psychologist, works jointly in evaluating maxillofacial defects both in the traumatic and congenital categories. The interchange of ideas from these different categories has greatly enhanced the rehabilitation of the patient. Our research in this field has been directed toward regeneration of the bony defects of the palate by electrical stimulation. Bone marrow grafts to restore skeletal anatomy of the mandible have been performed.

Our research is now directed towards determining the microanatomy of the muscles of the soft palate. An additional project utilizing cephalometric studies has been initiated to determine the effect of surgery on the developing maxilla in infants. This study will guide surgeons in selecting the appropriate surgery for maxillofacial reconstruction.

M4305.05-3017AGG2

COMPOSITE TISSUE TRANSPLANTATION. D.H.

McLean, G.A. LeBlanc and H. Buncke, Jr. Naval Hospital, Oakland.

The purpose of this project is to demonstrate the feasibility and advantages of partial limb and flap transfers in experimental animals. This is being accomplished through sterile microsurgery operative procedures on blood vessels and nerves of experimental animals.

The work will continue on dogs to anastomose the spermatic artery to the inferior epigastric artery, the pudendal artery or an omental artery. The purpose is to lengthen the spermatic artery to permit transplantation of the testicle into the thigh of the dog. Ultimate application to cryptorchid children is envisioned.

MR041.20.01-0241A2GX

SURGERY — THORACIC

CLINICAL EVALUATION OF IN-LINE FILTERS DURING EXTRACORPOREAL CIRCULATION.

P. Ah-Tye; R.G. Fosburg and M. Hartley. Naval Hospital, San Diego.

The effectiveness of commercially available in-line filters for extracorporeal circuits in reducing hemolysis, microemboli, and destruction of other blood elements will be studied in the laboratory. Dogs undergoing mitral valve replacement with homograft aortic valves without the use of in-line filters will be compared with series in which the Pall and Swank filters are used. Studies will include plasma hemoglobin, red cell fragility, platelet count, fibrinogens, protein determinations and lipid content.

CICC 2-16-410

USE OF THE MEMBRANE LUNG AS A RESPIRATORY SUPPORT SYSTEM.

P. Ah-Tye; M.J. O'Sullivan, Jr. and W.J. Storz. Naval Hospital, San Diego.

Membrane oxygenators will be utilized in the laboratory to develop a capability of prolonged respiratory support of experimental animals by partial perfusion techniques. Clinical trials will be initiated when sufficient and promising experience is obtained in this mode of support.

CICC 2-16-418

SEVERE HEMODILUTION TECHNIQUES FOR CARDIOPULMONARY BYPASS.

R.G. Fosburg; P. Ah-Tye and M. Hartley. Naval Hospital, San Diego.

Cardiopulmonary bypass accomplished with hemodilution to hematocrits averaging 10% might obviate or minimize the need for banked whole blood. Non-blood-containing priming fluids are employed in perfusion of dogs to achieve this goal. Appropriate studies to determine adequacy of perfusion, coagulation, renal function and body fluid compartments will be conducted.

CICC 2-16-408

THE CONTENT OF PERICARDIAL FLUID: EFFECTS ON HEMOLYSIS DURING CARDIOPULMONARY BYPASS.

R.G. Fosburg; T.L. Folkerth and M. Hartley. Naval Hospital, San Diego.

The role of pericardial fluid in altering blood elements during cardiopulmonary bypass is studied in the

animal laboratory. Analysis of blood directly aspirated from the pericardium is compared to the perfusate after transit through the cardiectomy reservoir and oxygenator. Appropriate samples are analyzed for plasma hemoglobin, osmotic fragility, free fatty acids, total protein, fibrinogens, fibrin split products and platelets. CICC 2-16-409

MANAGEMENT OF RESPIRATORY INSUFFICIENCY WITH A MEMBRANE OXYGENATOR.

J.J. McHale, Jr. and M. Mills. Naval Hospital, Bethesda.

We will evaluate the feasibility of supporting life with a membrane oxygenator. Pulmonary insufficiency causes death in a significant number of patients who might survive if their inadequate pulmonary function could be supported by an artificial lung. Conditions which can respond to temporary extracorporeal oxygenation with return of adequate lung function must be identified and documented.

Adult sheep have been oxygenated using several commercially available membrane lungs in 22 experiments lasting up to 96 hours. The volume of oxygen delivered and carbon dioxide removed was well above that necessary to support human life. One patient was successfully oxygenated for 20 hours with a membrane lung.

The use of extracorporeal perfusion with a temporary membrane lung should be considered in every case of severe self-limited pulmonary dysfunction where conventional means of support have clearly failed or are about to fail. Although exacting of personnel and equipment, adequate technology for temporary membrane oxygenator support is available, and the risk and morbidity appear to be reasonable.

M4305.05-3039AGC2

DEVELOPMENT OF A MILITARY RESPIRATOR.

M. Mills. Naval Hospital, Bethesda.

The need for excellent respiratory care in the management of combat casualties has led to the design of a portable, volume preset respirator to meet military specifications. Four engineering prototypes have been built under contract with the General Electric Corporation. They will operate in an intensive care unit under open-cycle conditions, accepting an outside source of power and oxygen. They will also operate under closed-cycle conditions employing a CO₂ scrubber, batteries, and a built-in oxygen source. Other unique features are: oxygen sensors for control and monitoring of FiO₂; mass flowmeters for control and

monitoring of volume delivery; and alarms for FiO_2 , expired volume and battery voltage.

These units have been tested on a lung model and on over 100 patients. Performance and safety are excellent. We conclude that it is feasible to produce a reliable, high-performance respirator for military use.
M4305.05-3027AGC2

THE EFFECTS OF MEDIASTINOSCOPY ON PULMONARY FUNCTION. J.V. Scutero and B.L. Aaron. Naval Hospital, Portsmouth, Va.

The study was posed to evaluate the effect of mediastinoscopy on pulmonary function.

The initial patients studied had bronchoscopies performed in conjunction with the mediastinoscopy, and the physiologic studies indicated a transient restrictive ventilatory defect.

Seeking to delete the effect of bronchoscopy, it is planned to evaluate a number of patients having only bronchoscopy and only mediastinoscopy. The results to date would indicate that no unusual or unexpected aberrations of pulmonary function result from this procedure.

MR041.20.01-0329A2GX

THE RECOVERY OF VENTILATION-PERFUSION (V/Q) FOLLOWING PNEUMOTHORAX. W.J. Storz; J.A. Gibbons and T.L. Folkerth. Naval Hospital, San Diego.

The time course of the return of V/Q after reexpansion of the lung, following a pneumothorax, is under investigation utilizing xenon scintiphotographic scanning. Serial determinations of V/Q by scintiphotography and arterial blood gas analysis are employed, upon expansion of the lung, by tube thoracostomy.
CICC 2-16-414

UROLOGY

TECHNIQUE FOR RAPID PARTIAL NEPHRECTOMY. O.W. Chenault and R.D. Dwyer. Naval Hospital, Portsmouth, Va.

A technique for rapid partial nephrectomy by sandwiching the involved renal tissue between two strips of dacron arterial-graft material is proposed. This technique permits early ambulation and vigorous endotracheal toilet with a lessened incidence of postoperative hemorrhage.

An experimental model subjecting dogs to bilateral partial nephrectomy, with this technique, has begun in an effort to ascertain the gross and microscopic effects of nonabsorbable materials in the urinary tract.
CICC 2-08-516

PROLONGED IMMOBILIZATION AND RENAL LITHIASIS. N.B. Cummings and F.R. Nelson. Naval Medical Research Institute, Bethesda.

Since an increase in renal lithiasis among casualties with prolonged immobilization has been observed, modified balance studies of men immobilized with single long-bone fractures were planned.

Eleven (ten femoral) fracture patients were studied. Patients ate a standard hospital diet. Measurements of 24-hour fluid intake and urinary output, electrolytes, 24-hour urinary creatinine clearance, calcium, phosphorus, hydroxyproline and pyrophosphate were made. Neither renal colic nor renal stone formation was observed. None of these patients had signs, symptoms or microscopic evidence of urinary tract infection. Urine volumes were maintained voluntarily at a high level (1200-3500 ml). Urinary hydroxyproline excretion was greater than levels reported on restricted diets. A modest hypercalciuria (50-200% greater than control levels) occurred at 1-3 weeks. Elevations of endogenous creatinine clearances, noted in the first month in all patients, ranged from 17 to 430% above top normal. Other values were within normal limits.

Since no renal lithiasis occurred in this group, a comparison of the above findings with those of patients with renal lithiasis is indicated.

MR041.20.01-0325A2HX

SUPRAPUBIC BLADDER DECOMPRESSION FOR URINARY RETENTION IN THE IMMEDIATE POST-OPERATIVE PATIENT USING A TWELVE-GAUGE INTERCATH. W.J. Fouty. Naval Hospital, Bethesda.

The specific aims of this study are to demonstrate a safe and inexpensive method for bladder decompression for urinary retention in the immediate postoperative period. Emphasis is to be placed on avoidance, or significant reduction in the incidence of urinary tract infection that frequently results from routine urethral catheterization.

It is hoped that the evidence will support routine adaptation of this procedure.

CICC 2-06-320

RELATIONSHIP BETWEEN SYSTEMIC AND RENAL HEMODYNAMICS IN SALT-RETAINING STATES BEFORE AND AFTER THERAPY. M.H. Humphreys and G.J. Weir, Jr. Naval Hospital, Great Lakes.

Patients with cirrhosis and ascites are known to retain sodium although the mechanism responsible for this sodium retention is unclear. Furthermore, a proportion of these patients may develop renal insufficiency in the absence of morphologic renal abnormalities.

One patient with alcoholic liver disease, jaundice and ascites had a 24-hour creatinine clearance of 80 ml/min, elevated renal plasma flow (RPF) (831 ml/min), and increased cardiac output (CO) (14.6 L/min). Another patient with more extensive liver disease had a creatinine clearance of only 9 ml/min associated with a diminished RPF, but with an elevated CO (10.5 L/min), although total peripheral resistance was similar in the two patients. Thus, the severe renal insufficiency observed in the second patient was related to a lowered blood pressure and total peripheral resistance but increased renal vascular resistance, while the normal renal function

observed in the first patient was marked by corresponding decreases in total peripheral resistance and renal vascular resistance.

CICC 2-13-015

EFFECT ON TESTICULAR HISTOLOGY OF TEMPORARILY AND PROLONGED VENOUS OCCLUSION AS OPPOSED TO SIMILAR TOTAL VASCULAR OCCLUSION. E.C. Sacher. Naval Hospital, Philadelphia.

Survival rates of dog testicular tissue were to be applied to human testes where various degrees of torsion of the spermatic cord had existed for various lengths of time.

The clinical investigation was terminated after delay in starting the project was caused by inadequate staffing. It was found that a similar project was being successfully completed at another institution. It is felt that duplication of the study is not warranted.

MR041.20.01-1382AGJ

We wish to express our appreciation for two excellent cover photographs provided by the Photography Division of the Medical Graphic Arts Dept., Naval Medical School, NNMC, Bethesda, Md. Photographer for the back cover picture was HM3 E.W. Larson, USN.

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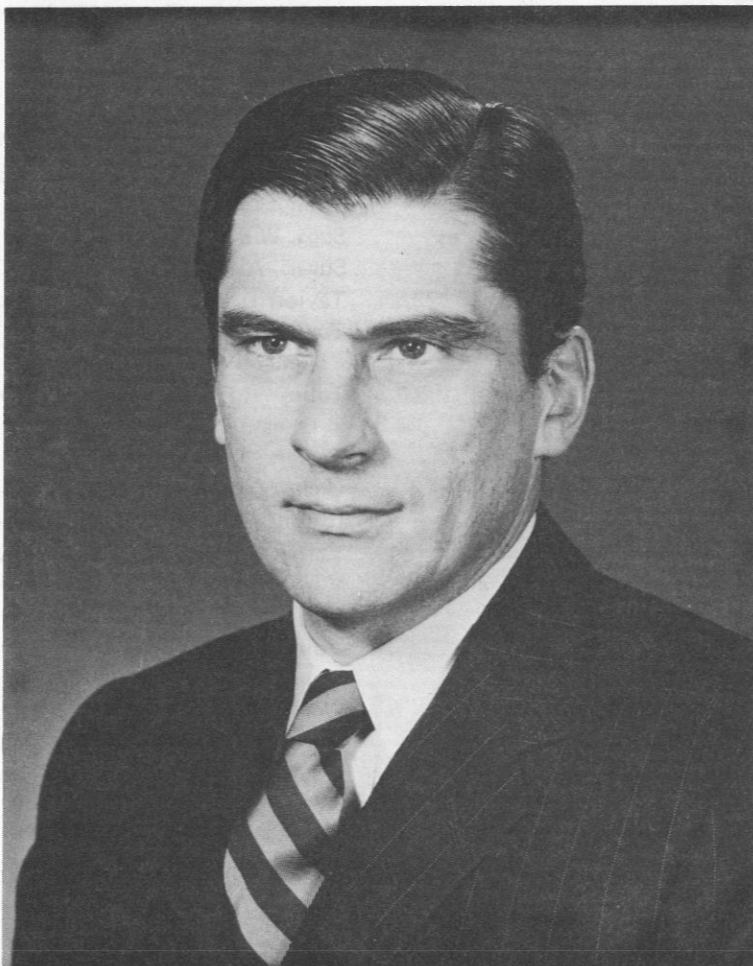
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NEW SECNAV SWORN IN



The Honorable John W. Warner, Secretary of the Navy

On 4 May 1972, John W. Warner was sworn in as the new Secretary of the Navy by Secretary of Defense Melvin Laird.

Mr. Warner was selected by President Nixon to succeed John H. Chafee who submitted his resignation in April. At the time of Mr. Chafee's resignation, Mr. Warner was serving as the Under Secretary of the Navy.

The first Navy Secretary to have served in both the Marine Corps and the Navy, Mr. Warner enlisted in the Navy in 1944 and was released from active duty in 1946 as an Electronic Technician Third Class. After having returned to school, he then became an officer in the Marine Corps Reserve. Called to active duty in 1950, Mr. Warner served as communications officer for two Marine Air Units in Korea.

To serve with Mr. Warner will be the Under Secretary of the Navy appointee, Mr. Frank P. Sanders. Mr. Sanders is resigning his post as Assistant Secretary of the Navy (Financial Management) to accept the new position.—NAVNEWS, Washington, D.C.

United States Navy Medicine

CORRESPONDENCE AND CONTRIBUTIONS from the field are welcomed and will be published as space permits, subject to editing and possible abridgment. All material should be submitted to the Editor, U.S. Navy Medicine, Code 18, Bureau of Medicine and Surgery, Washington, D.C. 20390

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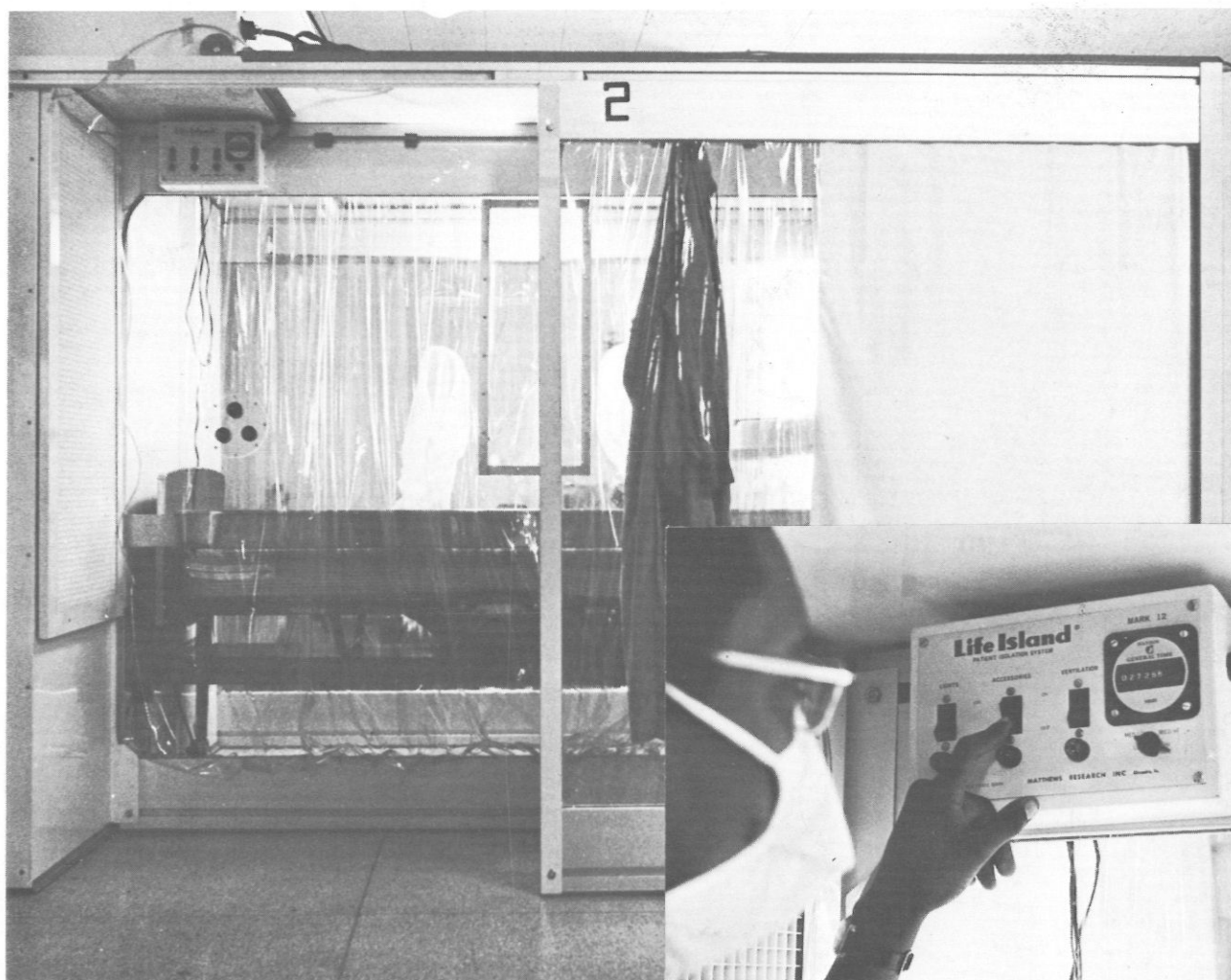
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